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SATURDAY MARCH 6 1954

TABLE OF CONTENTS

Yesterday and To-morrow in Child Health CHARLES MCNEIL, M.D., LL.D., F.R.C.P., F.R.C.P.Ed. 533

Anaemia in Kwashiorkor E. B. ADAMS, M.B., M.R.C.P. 537

Adrenocortical Function in Burned Patients SIMON SEVITT, M.D., M.SC., F.R.C.P.I., D.P.H. 541

The Achlorhydric Patient with Dyspepsia B. F. SWYNNERTON, D.M., M.R.C.P., and NORMAN C. TANNER, F.R.C.S. 546

Results of Treatment of Chronic Vasomotor Rhinitis.—Part I
PHILIP READING, M.S., F.R.C.S., and KENNETH MALCOMSON, F.R.C.S. 552

Results of Treatment of Chronic Vasomotor Rhinitis.—Part II
DESMOND O'NEILL, M.D., M.R.C.P., D.P.M., and KENNETH MALCOMSON, F.R.C.S. 554

Complications of Meckel's Diverticulum H. HASHEMIAN, M.B., F.R.C.S.Ed., and E. T. MURRAY, M.B., F.R.C.S. 556

Early Recurrent Acute Intussusception in Children D. A. MACFARLANE, F.R.C.S., and L. P. THOMAS, F.R.C.S. 559

Craniostenosis with Familial Vitamin-D-resistant Rickets E. N. COLEMAN, M.B., and J. B. FOOTE, M.D. 561

Anaesthesia in Hospital Breech Delivery
R. G. LAW, M.D., M.R.C.O.G., and SHILA G. RANSOM, M.R.C.S., L.R.C.P., D.A. 562

Dangers of Polypharmaceutical Preparations Containing Folic Acid CLIFTON P. LOWTHER, M.B., F.R.F.P.S. 564

MEDICAL MEMORANDA

Carbon Dioxide Retention Simulating Curarization. C. F. SCURR, M.B., D.A. 565

Possible Method of Pre-operative Anticipation of Thrombo-embolic Episodes. JOHN DUTTON, F.R.C.S. 566

BOOK REVIEWS 567

CLINICAL PATHOLOGY

Tests for Venereal Disease.—I. I. N. ORPWOOD PRICE, M.R.C.S., D.P.H. 575

GENERAL ARTICLES AND NEWS

NOVA ET VETERA 577

REPORTS OF SOCIETIES 577

MEDICAL NOTES IN PARLIAMENT 590

MEDICO-LEGAL 591

VITAL STATISTICS 592

QUESTIONS AND COMMENTS 595

OBITUARY

K. H. Digby, O.B.E., M.B., F.R.C.S. 586

F. R. Selbie, M.D., Ph.D., D.SC. 586

Eugene Wolff, M.B., F.R.C.S. 587

H. W. Pooler, M.D. 588

George Cooper, M.D., D.M.R.E. 589

R. W. Bollans, M.B. 589

E. Dorothy S. Price, M.D. 589

Balfour McKean, M.D. 590

LEADING ARTICLES

Child Life and Health 569

Q Fever 570

Measuring Hospital Efficiency 570

ANNOTATIONS

Cancer Registration 571

Burns and the Adrenal 572

Emotions and the Nose 573

Folic Acid and Pernicious Anaemia 573

Pyrazinamide with Isoniazid in Tuberculosis 574

The Clare Wand Fund 574

SUPPLEMENT

Full Contents on First Page of Supplement

The G.P. and the Health Visitor 61

General Medical Services Committee 62

Scottish News 64

Correspondence:

The Clare Wand Fund. S. WAND, M.B. 66

Remuneration of Hospital Medical Staff. W. A. BOURNE, M.D.; A. E. NICHOLLS, M.R.C.S.; D. J. R. STEEN, F.R.C.S. 66

A Bob a Job. M. J. OLDFIELD, M.B. 67

CORRESPONDENCE

Forceps in Obstetrics. T. N. A. JEFFCOATE, M.D. 579

Rh Antibodies and Domiciliary Midwifery. R. H. REYNOLDS, M.B.; C. W. WALKER, M.B.; E. S. WYDER, M.B. 579

Emphysema. J. G. MOORE, F.R.C.S.Ed. 580

Medical Needs in the Gold Coast. F. R. G. HEAF, F.R.C.P. 580

Lumbar Puncture. W. MCKISSOCK, F.R.C.S. 581

Ampoules. G. C. STEEL, F.F.A. R.C.S. 581

Blood Transfusion. G. DISCOMBE, M.D. 581

"Status Lymphaticus." W. B. LAING, M.B.; H. B. DODWELL, M.D.; A. V. NEALE, M.D. 582

Cortisone. J. H. LAURIE, M.B. 582

Anaesthesia. G. D. MCGRATH, D.A. 583

Controlled Hypothermia. H. C. CHURCHILL-DAVIDSON, M.D. 583

Unsaturated Fatty Acids. C. PETIT, L.R.C.P.I. 583

Iron. I. M. LIBRACH, M.B.; M. R. JEFFREY, M.D. 583

The Thyroid. T. LEVITT, F.R.C.S. 584

Thyrotoxicosis. E. MONTUSCHI, M.D.; H. F. W. KIRKPATRICK, Ph.D., and J. D. ROBERTSON, F.R.C.P. 584

College of General Practitioners. G. F. ABERCROMBIE, M.D., and J. H. HUNT, D.M. 585

Letters on other subjects appear on p. 585

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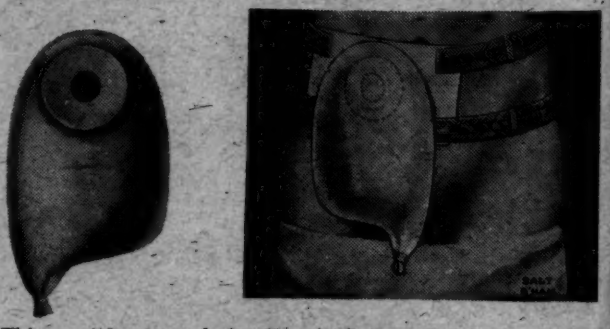

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 6 1954

YESTERDAY AND TO-MORROW IN CHILD HEALTH*

BY

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This address gives a short review in general terms of child health in the last hundred years. Although the examples and figures used in it have been drawn mainly from Scotland, the history has been much the same in England, Wales, and Ireland, and indeed far beyond these islands: it has been similar both in the measures taken to promote child health and in the results obtained. From such a historical survey we can get a perspective view of the growth of the subject and of its future progress.

The Infant Death Rates

Child health is a phrase full of meaning, but is so wide and deep in its meaning that it is difficult and perhaps impossible to define it. As an idea in the mind and as an object of human effort it is as old as the human family; and long before human records were kept the health and well-being of children must have been deeply cherished by their natural guardians, their fathers and mothers. But as a medical concept, and especially as a medico-social problem, it emerged in Britain about the middle of the last century; while the actual phrase—child health—obtained a recognized place in the medical vocabulary only about twenty years ago. It was the publication, for England and Wales in 1840, and for Scotland in 1855, of the numbers of births, deaths, and marriages, and of the population that drew attention to public health and to child mortality, for among these figures, called vital statistics, was included an infant death rate.

This infant death rate (or infant mortality rate) is the number of babies dying in the first year of life in every thousand who survive birth. These rates do not completely measure child mortality, for they omit the heavy loss of infants during birth (stillbirths), and also the considerable loss of children over 1 year of age. None the less, as these infant death rates rise and fall they fluctuate with the stillbirths and the deaths of older children; and they have long been accepted as giving in terms of death an index in reverse of the health of the child community. These infant death rates are given for the whole country and for its units of towns and country districts; so that if the infant death rates have fallen for one or over several years, we say that the state of child health in Scotland or in Glasgow is better; while if these rates have risen we feel that child health is worse. It is impossible to exaggerate the value of the infant death rates, which have now been published each year in Scotland for nearly a hundred years. These figure-measurements first disclosed the extent of child mortality; next they gradually uncovered the sinister and formidable league of causes that was producing such a wastage of child life; and then they brought into action, with slow and painful effort, various social and medical agencies to remove these causes. And now to-day, with a good deal accomplished in the reduction of child mortality, we tend to put still wider meanings into the phrase child health.

We realize that the child cannot be isolated as a person; and as we become aware of the connexions of child health with the fundamental social realities of family and home we see that child health in this wider context is at the centre of the nation's well-being. This wide conception of child health and the vision of its future fulfilment have been gradually reached by the use of the instrument of measurement that we have in the infant death rates.

Yesterday in Child Health

Let us look back over almost a hundred years of infant death rates in Scotland, for by giving the figures at the beginning and the end of the century we shall have a simple measure of the progress of child health in that time. The infant death rates for Glasgow for the same periods are added because later I make some remarks upon Glasgow, where the problem of infant mortality was perhaps more serious and more difficult than in any other large Scottish town. The infant death rates for Scotland and Glasgow were:

	1855–60	1952
Scotland	120	35
Glasgow	179	41

The figures speak for themselves and show a great reduction for Scotland and one relatively greater in the case of Glasgow. And the difference would be even greater if stillbirths were added; but stillbirths have been registered only in recent years. Even with incomplete figures we can see that in the last hundred years the tide of death has gone back a long, long way from the shore of infant life, or, to make a positive statement, that there has been a great gain in child health.

In running the eye over the figures in the years between the beginning and the end of the century a surprising fact becomes apparent. The great reduction over the century was not a steady downward trend

*The first G. B. Fleming Memorial Lecture, given in Glasgow on April 15, 1953. Dr. Geoffrey B. Fleming was Senior Physician at the Royal Hospital for Sick Children, Glasgow, and Professor of Child Health in the University of Glasgow from 1930 to 1947. The above address was prefaced by a tribute to his work and character.

throughout; there was nothing of the inevitability of gradualness about it. *In fact, the infant death rates in Scotland hardly moved down at all during the first fifty years of the century;* they fluctuated near 120; they rose to 130 in the 1891–1900 decade; and stood again at 120 in the 1901–5 period. But during the next fifty years (1906–52) the infant death rates have gone steadily down, with an acceleration since 1941. Is there any explanation of these tides of infant mortality remaining obstinately high for the first fifty years, and of their receding steadily during the next fifty years? We can answer the question only if we know something of the efforts that were being made to remove conditions hostile to infant life during the two periods. In any case the very different behaviour of the infant death rates in Scotland from 1855 to 1905 and from 1906 to 1952 justifies the division of our chosen "yesterday" into two periods of fifty years each.

It is interesting that in England and Wales the levels of infant death rates remained steadily high during the same 50-year period; indeed, they were at a higher level, remaining between 140 and 150. The English figures began to fall sooner than in Scotland. Presently they reached and then passed the Scottish levels, maintaining these lower levels until in 1952 the infant death rate in England and Wales was 28 and in Scotland it was 35.

The First Fifty Years: 1855–1905. Sanitation and the House

The first fifty years saw the first real beginning of sanitation as an organized community movement in Scotland; and naturally sanitary reform began in the largest towns. I take Glasgow as an example of the prevailing insanitary conditions in Scottish towns. Glasgow was first among Scottish towns for the size and density of her population, and was worst in her sanitary conditions. Her citizens were aware of these dangerous conditions; and in 1855, the first year of this first 50 years, the Loch Katrine Waterworks Act was passed which was to give Glasgow the finest water supply in the United Kingdom. This was followed by the creation of a sanitary department in 1862, and the appointment of her first medical officer of health the following year in the person of Dr. W. T. Gairdner, who was to become a distinguished physician. He was succeeded in 1872 by Dr. James Burn Russell, the second in a notable line of Glasgow medical officers of health. Before Russell took up his duties, great measures of sanitary reform had been carried out in water-supply, drainage, sewerage, removal of refuse, and paving, lighting, and cleansing of streets. The city as a whole and its streets had been cleaned up; but many thousands of its houses remained grossly insanitary. Russell held office till 1892; and he has left a record of sanitary and housing conditions in Glasgow during these 20 years, both in his official reports and in his addresses to the Glasgow Philosophical Society and other public audiences (Russell, 1905). These addresses were given to inform the citizens of what was happening in their midst, and to rouse their conscience to support official action and to engage in voluntary effort.

From the outset the new medical officer of health was convinced that further progress in Glasgow sanitation and public health would depend more than anything else on improvement of the housing conditions. He set himself to study the insanitary house. He listed the many ways in which a house could be insanitary—in structure, in sanitary conveniences, in lighting and ventilation, etc., and high on his list he placed overcrowding. He noted the effects of such houses on the men, women, and children who lived in them in terms of disease and moral degradation. He was a firm believer in the principle of measurement, and he applied it wherever he could. He was like the man in Ezekiel's prophecies: and he went into and through the houses of Glasgow "with a line of flax in his hand, and a measuring reed"—into the many-roomed mansions of Blythswood and the one- and two-roomed houses of Bridgegate. And he counted the number of persons who lived in each house. Thus after great labour he produced a house census for the whole city in which houses were graded according to the number of their rooms, the number of persons who lived in them, and the average air space for each person; and alongside these different grades of house he placed their general death rates and the infant death rates. All this work was embodied in official reports, but the gist of it was given to the citizens of Glasgow in these public addresses already mentioned.

These popular lectures give the classic account of the insanitary house, supplying the facts and figures, and adding vivid pictures of such houses and their effects upon their inhabitants. In a famous address, "Life in One Room," he told his audience that in 1881 the population of Glasgow was 511,520, and of this total 126,000 (a quarter) lived in one room, and 228,000 (nearly a half) lived in two rooms, and gave figures showing the high general death rates and the soaring infantile mortality rates in such houses. In another address, on "Uninhabitable Houses," he takes his audience inside "a one-roomed house . . . where there is no artificial light but a glimmer of light from a handful of red ashes, and going in one hears voices but sees no one, and 'where in the innermost recesses of the apartment, the air seems a residue of all the breath that had ever been breathed into it.'"

In 1891 Russell reviewed the progress of sanitary reform in Glasgow and for Scotland for the previous 30 years; he claimed that housing conditions had improved, giving facts and figures, and in support of his claims he showed the steady fall of the general death rates. But the fall in the infant death rates was trifling and insignificant, and these were to rise sharply in the next decade. He was sensitive about Glasgow's high infant mortality, and in another address he referred to this in one of his vivid phrases. Speaking of the quinquennium 1876–80 he says: "Glasgow makes away with 147 in every thousand of her children before she has had them in her fatal arms," but he notes with a kind of sad satisfaction that the infant death rate in Liverpool at the same time was 162.

Russell was a great man, and in his fight for sanitary reform in Glasgow he was single-minded, and concentrated his thought and effort on the dwelling-house as the final end of good sanitation. This task was a gigantic one and could not be finished in a single life, and when he died in 1904 much remained to be done.

Next year, 1905, saw the completion of 50 years of infant death rates in Scotland. I have already mentioned that the infant death rates remained steady throughout this period at 120 per 1,000, with small fluctuations; while the general death rates, starting at 20.7, had steadily fallen to 17 at the end (1901–5). In terms of health, we can say that the health of the whole population of Scotland, young and old, had become better in these 50 years; while the health of infants under 1 year remained at the same poor level. We know now that of all the death rates the infant death rate is the most sensitive to insanitary conditions; and by the end of this 50-year period (1855–1905) housing conditions in Glasgow and throughout Scotland had not reached a degree of improvement that was reflected in a lowered infant mortality, and during the same time no other effective aid, medical or social, was reaching mothers in their care of children inside these insanitary houses.

The Second Fifty Years: 1906–52. Mother and Child

In 1906, at the beginning of this second period, a national conference met in London to discuss infant mortality and measures for its reduction. The significance of this was that general attention was focused on the problem of infant mortality and its urgency. Still more significant were the words of Mr. John Burns, then President of the Local Government Board in England, in his address to the Conference: "Let us concentrate on the mother. What the

mother is the children are. . . . Let us glorify, dignify, and purify motherhood by every means in our power." In these words the Minister of State concerned with public health gave his blessing and support to efforts already being made, both by municipalities and by voluntary bodies, to assist mothers in their task of child care. I shall not overload this address with details of when and where in England and in Scotland milk depots, infant clinics, and schools for mothers were begun, but these agencies were already at work before 1906, fairly extensively in England, and here and there in Scotland. They were now extended; and they were gathered into a national system in the Maternity and Child Welfare Services Act of 1918. This Act might be described as a Special Education Act for Mothers; for its main benefits were that it provided mothers with teachers who gave them simple lessons in the care of their children.

I have already spoken of Dr. Russell, of Glasgow, and how he concentrated his effort on the good house as the end of sanitation in a well-governed city, and how he showed that bad houses brought disease and death to those within it, and especially to the children. But throughout the period of 50 years in which he lived bad housing was so widespread and deep-rooted that the movement of child health and also for general health was largely occupied with improving the sanitation of the city and of its houses. And now, in 1906, John Burns, of Battersea, spoke to the representatives of four nations and urged them to deal with the problem of infant mortality by *concentrating on the mother.* This is a simple phrase, but powerful in its wide and deep implications. For the mother is the housekeeper in a double sense, keeping both the house and her children and husband. The sanitary department does not sweep and clean her house, and the doctor and nurse do not feed or wash her baby. And when John Burns added, "What the mother is, the children are," he was stating in simple words a great truth, and indeed was filling in almost the whole truth of infant and child health. The two foundation stones of child health are a good house and a good housemother. And of a good mother much is required: a good conscience, both a sanitary conscience towards her house and all its materials, and a maternal conscience towards her children; a mind that *knows* how to keep the house clean and how to feed her baby; and a strong body and capable hands.

These are the abstract principles that govern the life and health of the mother and her children; and now we can speak of practical results. This advice to concentrate on the mother has been followed out for the last 50 years; and it has given a better understanding of her problems, separating the things that must be done for her from the things that she alone can do. It has strengthened services already at work, and has brought new services into action.

The care of the mother's general health and her careful supervision in pregnancy and in her confinement have been undertaken in the new service of antenatal clinics which have strongly reinforced the work of the maternity hospitals. The combined antenatal–maternity service has reduced maternal deaths, has raised the level of health in mothers, and has also reduced infant deaths during birth and in the first month after birth.

At the same time the care of the sick child has been greatly improved by increased accommodation in children's hospitals, by the building of new hospitals and especially of fever hospitals, and by advance in knowledge of disease in children and in the power of its treatment. This better knowledge of disease in children, put at the disposal of family doctors and practised in the home, has also strengthened the general service of the sick child.

Education of the Mother in Child Care

This had begun in a feeble and scattered way before the second period of 50 years had opened; and it was firmly established only in 1918 by the inauguration of the child welfare service. This was a new and great enterprise; an attempt on a national scale to provide the mother with education in all the tasks of child care which she alone can give. The doctors and health visitors were the teachers, giving their lessons at the infant clinics and inside the homes; but the practice of these lessons in child care rested in the instructed mind and in the strong and willing hands of the mother in her home.

The important part of this education was in the feeding of infants and in domestic sanitation. Infant-feeding had long been a subject of study in children's hospitals; and it was mainly a study of the use of clean cows' milk as a substitute for breast milk. At first cows' milk mixtures were complicated, and the instruction in their use reached mothers only indirectly or not at all. But by the time the new child welfare service was begun the use of cows' milk for infants had been much simplified, and instruction was now given by an army of teachers, and directly into the ears of mothers. For the young baby, the right use of cows' milk is a matter of life and death, and thousands of infant lives must have been saved by this national education of mothers in infant feeding.

The Children's Hospitals

The teaching children's hospitals had always had a double function—the advance of knowledge of disease and its treatment, and the study of health and the instruments that secure it; and the courses of instruction both in disease and in health were steadily extended and given to increasing numbers of medical students. Further, the establishment of chairs and departments of child health, first in Glasgow in 1924 and later in Edinburgh, Aberdeen, and St. Andrews, took place in this period and strengthened the status of the subject in all the four Scottish medical schools; while the title of child heath encouraged teaching and study in the whole field of child medicine.

I have given a short account of the more important results that have followed the London Conference on Infantile Mortality in 1906, with its slogan, "Let us concentrate on the mother." Throughout this second period of almost 50 years the work of sanitation and of replacing bad houses with good ones went on. The building of new houses was seriously interrupted during the two wars; but since 1945 it has been resumed, and at a greater pace than ever before. In addition, great attention has been paid to the mother and her children; old services of hospital care for mother and child have been extended and strengthened, and the great new experiment of education of the mother in her own care of her children has had a full trial of 30 years. In short, much effort has been made both for better houses and for the betterment of the mother and children who live in them. Under this combination of effort what progress has been made in child health, measured by infant death rates? The figures for the first quinquennium of the period under review (1906–10) and for the last completed year, 1952, are given for all Scotland, and for Glasgow; and will answer the question.

	1906–10	1952
Scotland	112	35
Glasgow	130	41

This fifty-year period began with a slight improvement; and this continued steadily throughout, with an acceleration since 1940, and reached low levels in 1952. There can be no doubt that in the second 50 years there has been a great improvement in child health. While most of us will agree that improved housing, the education of mothers in child care, and the better hospital care of the mother and the sick child have each played a part in the result, there may be argument about the order of their importance.

Near the end of his work in Glasgow James Russell, still grappling with his unfinished task of improving housing conditions, made a remarkable statement, a prophetic statement, but with no date of its fulfilment. "I see nothing in the nature of things," he said, "why life in the town should not be as healthy as the country." Within 50 years of his death in 1904, his prophetic hope has been realized in the infant death rates for Edinburgh and Aberdeen, and

almost realized for Glasgow. In 1952 the infant death rate for all Scotland was 35 : for her rural areas it was 33, for Edinburgh 29, for Aberdeen 30, and for Glasgow 41. When we consider the factors of size and density of population, the presence of "heavy industries," and the legacy of insanitary houses, Glasgow's present low infant death rate entitles her to the place of honour among the larger Scottish towns.

To-morrow in Child Health

We have looked back over a hundred years of work for child health, and have noted the great progress made in the past 50 years. The ideas and the acts of this long yesterday will be carried forward into to-morrow. What are the prospects, immediate and more distant?

Let us name the list of the existing services of child care. They are communal and domestic sanitation ; the antenatal, maternity, and neonatal services ; the children's and fever hospitals ; the child welfare service ; family doctors ; and, greatest of them all, the home service of mothers. This great array of agencies and their increasing efficiency will ensure in the lengthening years of to-morrow a continuing and steady reduction of the existing rates of infant deaths. A few examples will show the low levels of infant death rate that have already been reached : England and Wales (1952), 28 ; Holland (1951), 25 ; New Zealand (1951), 23 ; and Sweden (1951), 20. These rates do not measure the total infant loss, but this total loss can be obtained when stillbirths are added, and the total sum of infant deaths is divided into the two main groups of the early "catastrophic" deaths and the later "careless" deaths. Thus for New Zealand, in 1951, the first group of natal–neonatal deaths—that is, including stillbirths—gave a total death rate of 40, and the second group of deaths in the first year (after the first month) gave a rate of 7.

The Irreducible Minimum of Infant Deaths.—A closer examination of these record low levels of total infant loss shows that further reduction is still possible, until the irreducible minimum is reached, made up by the inevitable hazards and accidents of infant life ; and we may be sure that the larger fraction of this minimum will lie in the natal–neonatal group. In 50 years' time, or longer, we might expect from one or two countries such rates of total infant loss as 20 for the natal–neonatal group, and 5 for the 11 succeeding months of the first year. But this attainable optimum will be reached only through the steady pressure and increasing efficiency of the services of child care.

I shall now give some notes upon each of these services of child care and upon their future contribution to child health.

Sanitation and Housing.—Only a few words are required on this subject. Local authorities and their medical officers of health know better than anyone else the importance of keeping general sanitation in all its aspects at the highest level, and of improving housing conditions and building new houses. Bad houses remain, but they are few in comparison with the thousands that Dr. Russell counted in Glasgow in his famous survey of 1881. Overcrowding remains, but the pace of building new houses increases year by year. And let us not forget that the fruit of good sanitation can be brought to perfection only by good houses and *good housekeepers.*

Antenatal, Maternity, and Neonatal Services.—This triple service is expanding in each of its branches. It grapples with difficult problems both in mother and in child, and with a high infant loss during birth and early infancy. The reduction of the maternal and infant death rates in the last two decades is the proof of its success. A further reduction in deaths from prematurity is certain to continue, both from the preventive work in the antenatal clinics and from the extending special care of premature newborn babies.

Children's and Fever Hospitals.—The future contribution of these hospitals will be mainly in curative medicine, in the diagnosis and treatment of serious illness, and in the deep study of the many problems of disease that remain unsolved. Their teaching hospitals are well supplied with material of disease in childhood, but they lack the clinical material and experience of healthy infants and children. This lack of material can be supplied in the clinics of the child welfare service.

Future of the Child Welfare Service: Provision of Training Schools

The curative work of the service in the treatment of many kinds of minor disorder and in the diagnosis of serious illness at the clinics is of great value. But more valuable is its preventive work. This has a double aim—(1) to reduce to a minimum the number of infant and child deaths, and (2) to raise to a maximum the quality of life in the survivors—and a single method of achieving it by the education of mothers in the manifold kinds of child care and in the right use of each.

The two aims of this young child welfare service are an immense task. The first aim—the mastery of fatal disease in infants—has gone a long way towards achievement ; the second aim of maximum health in childhood is only beginning, and its full accomplishment can come only in the far-distant future. Here and there suggestions are heard that, with the great reduction of the infant death rates, the personnel and work of the child welfare service may now be cut down, and that a partial demobilization in the civil war against disease in children might now take place. But there is no discharge in this war ; the death rates must still be kept down, and the new campaign of raising levels of health in children is only beginning. And for this longer and more difficult campaign the child welfare service must be strengthened and given new and better weapons.

The most important work of the service is the education of mothers in the care of children. For this its doctors and nurses require better training than they now receive. There is an urgent need for the provision of training-schools in infant child health, these to be located in child welfare clinics. At present the doctors of the service get their training in child health in a children's hospital as part of the course of teaching in diseases of children. But the children's hospitals lack the essential clinical material of mothers and healthy infants and children, Such material, both for study and for training, can be provided only in a child welfare clinic, and, best of all, in one attached to a maternity hospital where the clinic has a close link with the nurseries of the newborn. I have already given the argument in favour of this proposal (McNeil, 1945) in an article "The Clinical Material of Child Health : where to obtain it ; and how to use it." This argument was based on my conduct of such a clinic in Edinburgh for 17 years, and upon a teaching course in infant and child health given to medical students at the Maternity Pavilion, University of Edinburgh. This personal experience has convinced me that the most immediate and important need for the child welfare service is the provision of centres of study and schools of training in child health. These would, I believe, do for the new service what the use of hospitals for the study and teaching of disease has done for the medical practice of disease in children. The child welfare service with its own training-schools would steadily gain in power, authority, and prestige.

The Home Service of Mothers

The work of the mother for her children at home is the foundation and centre on which all the other activities of child care are built. In 1906 John Burns said: "Let us concentrate on the mother. . . . Let us glorify, dignify, and purify motherhood by all means in our power." These words set a target that is still far from being reached. But they turned the attention of medical and social reformers from the circumstantial *things* of child care—sanitation and the house—and towards the central *persons*—the mother and child at home ; and they created in the child welfare service a national system of education of mothers in child care.

Fifty years later infant mortality, the subject of the London conference in 1906, has been brought under strong control in many countries, and to this massive achievement the new service of education has made an indispensable contribution. But great, difficult, and unfinished tasks of promoting the health of infants and children remain; and these tasks will lie largely in the hands of the child welfare service.

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ANAEMIA IN KWASHIORKOR

BY

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Kwashiorkor has been defined by Brock and Autret (1952) as a nutritional syndrome of African infants and children comprising retarded growth, alterations in skin and hair pigmentation, oedema, fatty infiltration, cellular necrosis or fibrosis of the liver, and frequently a variety of dermatoses. Mortality is heavy in the absence of proper dietary treatment.

The anaemia often found in kwashiorkor is usually mild in degree, normocytic or slightly macrocytic, and has responded somewhat slowly during treatment of the syndrome by high-protein diets (Altmann and Murray, 1948; Trowell *et al.*, 1952). In East Africa, where tropical infestations are common, sometimes there is hypochromia, responding to iron treatment; often there is slight macrocytosis, but megaloblastic change rarely if ever occurs (Trowell, 1949). Lehmann (1952) believes that this macrocytosis without megaloblastic change is due to the presence of reticulocytes following blood loss. In Johannesburg, where parasitic infestations are infrequent, Altmann and Murray have observed a more constant blood picture. They considered anaemia to be due to deficiency of protein. Three of their 34 cases showed macrocytosis, while others became macrocytic on high-protein diets. In the marrow smears of six cases abnormal cells were seen suggestive of lack of liver principle or folic acid, but, as Trowell has also observed, the red-cell precursors were of an intermediate type or macronormoblastic, there were some giant metamyelocytes, but true megaloblasts of Ehrlich were not seen. Walt *et al.* (1950) also record a moderate, slightly macrocytic normochromic anaemia in their cases in Durban. In three, all fatal, anaemia was severe, but there was no megaloblastic change. Macrocytosis was reported by van der Sar (1951) to be common in his 31 cases of kwashiorkor in Curaçao, but in only one was the bone marrow megaloblastic.

It is now generally accepted that the syndrome is due to deficiency of protein in the diet, and that it responds well to treatment with high-protein diets, anaemia slowly improving at the same time. It is said that the anaemia does not respond to folic acid, vitamin B_{12}, or liver extracts (Trowell *et al.*, 1952), although Piéraerts (1950) believes it will respond to these after protein replacement.

The possible relationship of this anaemia to protein deficiency, the occurrence of macrocytosis, and the reports that in the bone marrow there are features of megaloblastic change without the full picture seen in megaloblastic anaemias have prompted the present investigation, in which haematological findings in a series of cases of kwashiorkor are described.

Clinical Material

Twenty-one cases have been studied—nineteen of African and two of Indian origin. The ages ranged from 1 to 5 years, with a mean of 2 years 3 months. Eleven were male and ten female.

In each case pitting oedema, dermatosis, and lowered plasma proteins were present. With the absence of complicating diseases these were the only criteria used in the selection of cases. Pitting oedema was always found in the legs and usually in the hands. Often facial oedema and generalized anasarca were marked. The dermatosis was similar to that described by Gillman and Gillman (1951) and by Brock and Autret (1952). Total plasma proteins ranged from 3.5 to 4.9 g.%, with a mean of 4.05 ± 0.10 g.%, and the albumin fraction from 1.2 to 2.6 g.% about a mean of 1.89 ± 0.04 g.% (see Table I).

TABLE I.—*Plasma Proteins Before and After Treatment, and Plasma Bilirubin on Admission*

Case No.	On Admission			After Treatment	
	Total Protein (g.%)	Albumin (g.%)	Bilirubin (mg./100 ml.)	Total Protein (g.%)	Albumin (g.%)
1	4·3	1·6	0·9		*
2	4·0	—	0·9	6·7	4·0
3	3·8	1·8	0·2		*
4	4·0	1·7	0·1	6·3	3·6
5	4·4	2·1	0·2	7·0	4·0
6	3·8	1·5	0·3	7·5	3·8
7	3·5	1·6	0·2	—	—
8	4·9	2·2	0·2	5·9	3·9
9	3·5	2·3	0·3		d
10	3·5	2·3	0·4		*
11	4·7	2·4	0·3	5·8	3·6
12	3·5	1·7	0·7	8·2	4·3
13	4·9	2·6	0·3	5·8	—
14	3·5	1·9	0·5	7·0	4·0
15	3·8	1·2	0·3		*
16	3·8	1·9	0·4		*
17	3·5	1·5	0·4		d
18	4·5	1·9	0·3	6·7	3·8
19	4·4	1·7	0·3		d
20	4·1	2·0	0·3		*
21	4·6	1·8	0·3		*
Means	4·05 ±0·10	1·89 ±0·04		6·70 ±0·23	3·89 ±0·07

d = died. * = removed from hospital before recovery complete.

No case was included without all these features, but other manifestations of the syndrome such as mental apathy, retardation of growth, and thinning of the hair with reddish pigmentation were present in varying degree. The liver was enlarged in 12 cases. In none was the spleen palpable. Abnormalities were not detected in the heart or nervous system, and lymph nodes were never enlarged. No specific changes were observed in the tongue although it was sometimes red, and there were no significant lung changes clinically or on *x*-ray examination except in two of the fatal cases which showed radiological evidence of bronchopneumonia.

Stools were sometimes watery and occasionally oily, but diarrhoea was not a marked feature. Stools were always examined, usually on three consecutive days. *Entamoeba histolytica* was isolated in two cases, but there was no dysentery. Ova of ascaris were observed in three cases, while in one of these there were hookworm ova, but here the test for occult blood was negative. This low incidence of parasites indicates the small chance that intestinal infestations were responsible for the anaemia in this series.

Plasma bilirubin was estimated in every case, but in none was it elevated (see Table I).

Treatment consisted of soured milk (maas) or this and a hydrolysed protein preparation ("casydrol") given in alternate feeds until convalescence, when ward diet was added.

Eleven patients made an excellent recovery, with disappearance of all symptoms, loss of oedema and skin changes,

and gain in weight and vitality. Hair changes often persisted. Three children died, permission for necropsy being refused. Seven were removed from hospital against advice before recovery was complete. There was a return of total plasma proteins and albumin to normal values in all cases, with complete clinical recovery except in one in which a final estimation was not made (see Table I).

Methods

Blood was obtained from the jugular veins in all cases, and all haematological investigations were done by me, using dry sterile syringes with ammonium and potassium oxalate as anticoagulant. Haemoglobin was determined by a photometric method. Packed cell volumes were estimated in duplicate and red cells counted in a double chamber filling. Reticulocytes were counted by the method of Dacie (1950). Aspiration specimens of iliac marrow were obtained from every case by iliac puncture and stained with May–Grunwald–Giemsa. Mean corpuscular diameters were measured by the method of Price-Jones (1933).

The Anaemia

On admission most cases showed only mild anaemia. Often, however, there was a drop in haemoglobin, red cells, and packed cell volume in the first week, although this sometimes occurred later. This drop took place without evidence of haemolysis or blood loss. If the lowest haemoglobin levels recorded are examined it is seen that the degree of anaemia encountered in these cases is not so mild. In 14 cases haemoglobin was below 9 g.%, while in six it was less than 7 g.% (see Table II).

White-cell counts tended to be high, with a range from 7,450 to 19,200 per c.mm., about a mean of 12,700 per c.mm. but otherwise they usually showed no departure from normal. Platelets always appeared to be plentiful and platelet counts were not done.

Hypochromia was seen only once—in Case 14 after treatment, when it was of mild degree. Mean corpuscular haemoglobin concentrations varied from 26 to 36%, with a mean of 31%.

Examination of the bone marrow showed normoblastic erythropoiesis in 13 cases and in these there were no abnormalities in the myeloid series. In the remaining eight cases the marrow deviated from normal in varying degree. In two there were some megaloblasts of Ehrlich as well as normoblasts and giant metamyelocytes (Cases 17 and 20). There were also macronormoblasts, some of which had nuclei with several lobes. The bone marrow in the other six cases showed a few giant metamyelocytes and occasional macropolycytes. The red-cell precursors were mainly normoblastic, but a few showed megaloblastic features. In these the cartwheel appearance of the nuclei was absent, a finer chromatin structure taking its place. They are presumably the cells described by Altmann and Murray as being of intermediate type. Premature haemoglobinization was sometimes seen; fully haemoglobinized erythroblasts were sometimes large, occasionally with lobed nuclei, but orthochromatic megaloblasts were not seen.

These cases with bone-marrow abnormalities appear to form a series, at one end of which the marrow is almost normal with only giant metamyelocytes, while at the other there is some definite megaloblastic change.

Cell Size

There was mild macrocytosis in 11 cases in which the mean corpuscular volume was above 100 μ^3. It did not appear to be related to the bone-marrow changes just described: in those with normoblastic erythropoiesis the mean was 98.0 ± 2.7 μ^3, while in the group with abnormal marrows there was a mean of 103.9 ± 2.8 μ^3, the difference not being significant (see Table II). In most of the blood films the red cells appeared somewhat large, with some anisocytosis, but little poikilocytosis. Even in the two patients with partial megaloblastic change, the cells in the blood films were round, but in one anisocytosis was marked (Case 17). This is demonstrated in the Price-Jones curve from this case, which shows broadening of the base and macrocytosis (see Fig. 1). Less variation was observed in other cases. There was some macrocytosis even in cases

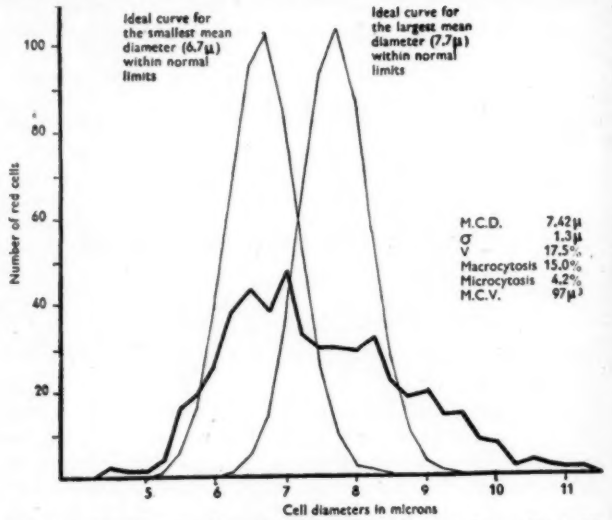
Ideal curve for the smallest mean diameter (6.7μ) within normal limits
Ideal curve for the largest mean diameter (7.7μ) within normal limits
M.C.D. 7.42μ
σ 1.3μ
V 17.5%
Macrocytosis 15.0%
Microcytosis 4.2%
M.C.V. 97μ³
Number of red cells
Cell diameters in microns

FIG. 1.—Erythrocyte diameter distribution curve from Case 17.

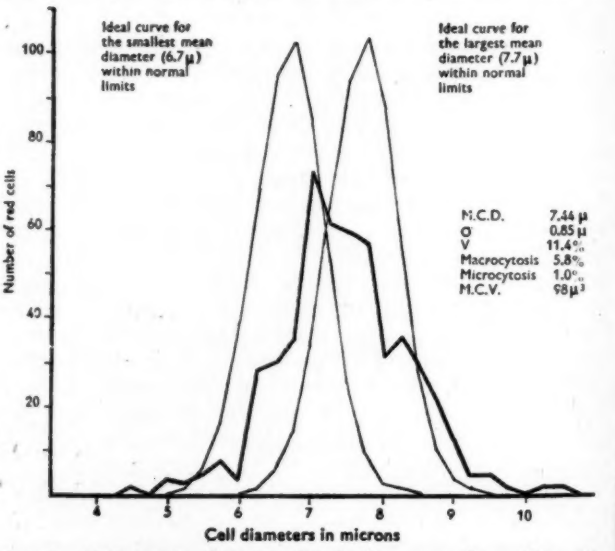
Ideal curve for the smallest mean diameter (6.7μ) within normal limits
Ideal curve for the largest mean diameter (7.7μ) within normal limits
M.C.D. 7.44μ
σ 0.85μ
V 11.4%
Macrocytosis 5.8%
Microcytosis 1.0%
M.C.V. 98μ³
Number of red cells
Cell diameters in microns

FIG. 2.—Erythrocyte diameter distribution curve from Case 16.

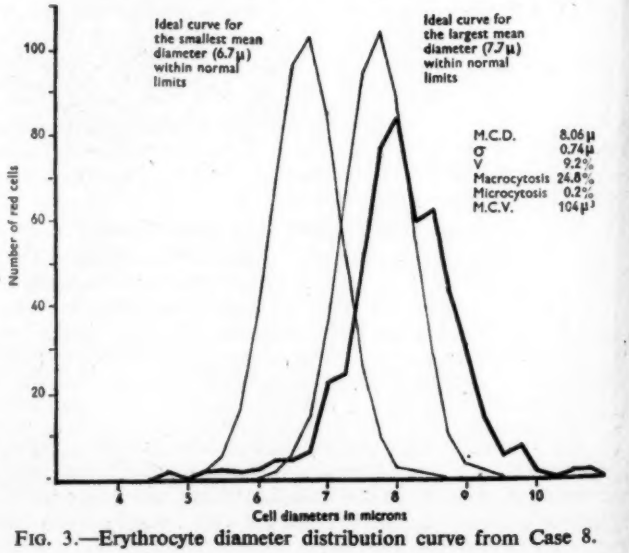
Ideal curve for the smallest mean diameter (6.7μ) within normal limits
Ideal curve for the largest mean diameter (7.7μ) within normal limits
M.C.D. 8.06μ
σ 0.74μ
V 9.2%
Macrocytosis 24.8%
Microcytosis 0.2%
M.C.V. 104μ³
Number of red cells
Cell diameters in microns

FIG. 3.—Erythrocyte diameter distribution curve from Case 8.

with normal marrow—for example, Case 16, in which the M.C.V. was 98 μ^3, the mean of the group (see Fig 2)—and in others with giant metamyelocytes and some intermediate red-cell precursors—for example, Case 8 (Fig. 3). Reticulocytosis did not seem to be the cause of the macrocytosis in any of these cases.

TABLE II.—*Blood Counts on Admission and After Recovery, and Lowest Haemoglobin Recorded*

Case No.	On Admission						Lowest Hb (g./100 ml.)	After Recovery		
	Hb (g./100 ml.)	Red Cells (mil./c.mm.)	M.C.V. (μ^3)	M.C.H.C. (%)	Retics. (%)	White Cells (per c.mm.)		Hb (g./100 ml.)	Red Cells (mil./c.mm.)	M.C.V. (μ^3)
Cases with Normal Bone Marrow										
1	10·5	3·21	106	31	3·5	14,600	9·0	10·2	2·86	114*
2	7·9	2·42	124	26	7·1	15,600	6·6	10·6	3·97	94
3	8·2	2·78	103	29	0·6	13,100	8·2			*
6	10·5	4·33	83	29	0·7	13,500	8·9	9·5	4·07	85
7	8·2	2·80	94	31	2·3	12,500	8·2			
9	6·3	2·24	89	32	1·4	18,400	6·3			d
10	11·2	3·55	94	33	0·9	7,450	11·2			*
11	11·5	3·67	99	32	2·7	9,150	11·5	12·2	3·26	116
13	12·0	3·76	92	35	2·9	10,500	12·0	11·9	3·37	110
14	10·8	3·76	90	32	1·2	7,600	6·1	11·2	4·51	79
15	10·5	3·20	100	33	0·7	11,900	10·5	10·6	3·55	101*
16	8·6	3·15	98	28	1·7	9,150	7·3			*
21	10·2	3·20	102	31	2·1	15,450	9·7			*
Cases with Abnormal Bone Marrow										
4	7·7	2·58	107	28	3·0	11,050	7·6	9·4	3·23	102
5	9·5	2·52	119	32	0·3	19,200	8·7	10·6	3·73	97
8	6·6	2·06	104	30	2·6	9,550	4·7	13·0	3·95	96
12	9·0	2·46	102	36	3·0	16,400	6·8	11·7	3·85	100
17	5·5	1·95	97	29	2·9	16,500	5·5			d
18	10·0	3·45	90	32	1·6	9,900	8·6	11·9	4·51	85
19	9·5	2·97	104	31	1·9	16,000	7·1			d
20	10·8	3·18	108	31	1·1	9,950	10·8			*

d=died. *=removed from hospital before recovery complete.

Case Histories

(i) Normoblastic Anaemias

In this group of 13 patients, the bulk of the series, anaemia was usually mild, although in one child who died haemoglobin on admission was only 6.3 g.%. The mean haemoglobin on admission was 9.7 g.%, while in the seven cases that recovered completely the mean on discharge was 10.9 g.%. Folic acid was used in one and vitamin B_{12} in another without effect, and ferrous sulphate was ineffective in both. Usually the anaemia increased in severity while the condition of the child improved in all other respects, the blood count after full recovery being slightly higher than on admission, as illustrated by the following example.

Case 14.—An African girl aged 3 years was admitted with gross oedema and patchy pigmentation and desquamation of the groins. Plasma proteins were 3.5 g.%, with 1.9 g.% albumin. Haemoglobin was 10.8 g.%, with 3,760,000 red cells per c.mm., haematocrit 34%, reticulocytes 1.2%. The bone marrow was normoblastic. On maas diet only oedema disappeared in three weeks—when plasma proteins had reached 5.3 g.%, with 3.2 g.% albumin. Hb was then 8.6 g.%, but despite general improvement the blood count dropped steadily. Injection of 50 μg. of vitamin B_{12} had no effect. The lowest count was 6.1 g.% Hb, 2,360,000 red cells per c.mm., haematocrit 21.5%, while at the same time plasma proteins were 7 g.% and albumin 4 g.%. Slight hypochromia was now observed in the blood film. Later ferrous sulphate was given by mouth, although the count had already begun to rise. The rate of increase did not appear to be altered. When the child had fully recovered the Hb was 11.2 g.%, red cells 4,510,000 per c.mm., and haematocrit 35.5%.

(ii) Anaemias With Giant Metamyelocytes and Some Red-cell Precursors of Intermediate Type in the Bone Marrow

In this group of six cases the effect of diet only was observed in three. In one with 7.7 g.% Hb on admission (Case 4) anaemia slowly decreased as the child recovered, the Hb reaching 9.4 g.%. The haemoglobin of another with 10 g.% on admission dropped to 8.6 g.% in four days, rising slowly to 11.9 g.% when clinical recovery was complete (Case 18). Reticulocytes, counted daily for two weeks, reached a peak of 7.2% on the ninth day. The fourth child (Case 19) was admitted with 9.5 g.% (haematocrit 31%), which dropped rapidly to 7.1 g.% (haematocrit 22%) on the sixth day, when he died. There was a peak reticulocyte count of 2.8% on the third day.

One child was given folic acid five weeks after admission. Haemoglobin was rising slowly on diet alone, and there was no reticulocyte increase.

In contrast, two patients with similar bone-marrow pictures responded to treatment with a crude liver extract and vitamin B_{12}.

Case 8.—An African child aged 20 months was admitted with a two-weeks history of swelling of the whole body, vomiting after feeds, anorexia, cough, and passing soft yellow stools. The temperature was 101.6° F. (38.7° C.), pulse 120, and respirations 20, weight 14½ lb. (6.6 kg.). There was marked oedema of the arms, legs, and face, and a red tinge of the hair. Black-pigmented skin changes were present in the inguinal region, with central desquamation, and there were similar lesions on the legs. The mucous membranes were pale. The liver and spleen could not be felt and there were no other abnormalities. The Hb was 6.6 g.%, red cells 2,060,000 per c.mm., haematocrit 21.5%, reticulocytes 2.6%, leucocytes 9,550 per c.mm. (the Price-Jones curve from this case is shown in Fig. 3). The bone marrow was mainly normoblastic, but there were some giant metamyelocytes and the nuclear structure of a minority of the basophil erythroblasts was rather fine. Plasma proteins were 4.9 g.%, albumin 2.2 g.%, bilirubin 0.2 mg. per 100 ml. No pathogens were detected in six stool specimens. The test for occult blood was negative. Urine was normal. *X*-ray examination of the chest showed marked striations in the right middle lobe, but the Mantoux test was negative, and *x*-ray films showed no change three weeks later. Free acid was present in the gastric juice after histamine.

On high-protein diet alone reticulocytes reached 5.8% on the fifth day, and oedema began to decrease. After two weeks, however, there was rapid deterioration; on the 17th day the Hb was only 4.7 g.%, with 1,370,000 red cells per c.mm., and haematocrit 15.5%. No reticulocytes were seen. 150 ml. of compatible blood was transfused and 1 ml. of a crude liver extract (" pernaemon ") given by intramuscular injection. Seven days later there was a reticulocyte peak of 10.4%.

Two further injections of the same liver preparation were given, the blood count rising steadily to 13.7 g.% Hb in seven weeks, with 4,580,000 red cells per c.mm., and haematocrit 45%. Plasma proteins were 5.9 g.%, albumin 3.9 g.%. There was now no oedema, skin changes had disappeared, and the child was well and happy.

Case 12.—An African infant aged 4 had the same pattern of disease. Anaemia became more severe as oedema subsided and plasma proteins increased, although there was again no haemolysis or blood loss. The admission Hb of 9 g.% dropped in seven days to 7 g.%, with 1,880,000 red cells per c.mm., haematocrit 21.5%, and reticulocytes 2.3%. There was histamine-fast achlorhydria. Injection of 50 μg. of vitamin B_{12} was followed in six days by a reticulocyte peak of 12.7%, and the blood count increased on this and further injections of vitamin B_{12} to reach 11.7 g.% Hb, 3,850,000 red cells, and haematocrit 38.5% on full recovery.

(iii) Megaloblastic Anaemias

There was megaloblastic change in the bone marrow of two infants. In one, who was removed from hospital against advice, there were many typical megaloblasts of Ehrlich and giant metamyelocytes in the marrow (Case 20). These changes were present but less well marked in the other (Case 17), who died, so it was not possible in either to observe the response of the anaemia to treatment.

Case 17.—A male African child of 18 months was admitted with a history of swelling of the body for one month, loose stools, and a cough for two weeks. His diet had consisted entirely of samp porridge and tea. His temperature was 100.4° F. (38° C.), pulse 112, respirations 22, weight 18 lb. (8.2 kg.). He was listless and apathetic, with gross swelling of the whole body and pitting oedema of the limbs and trunk. Facial oedema had occluded one eye. The hair was fine in texture and reddish brown. Widespread dermatosis was present, with scaling on the limbs and lower trunk, large areas of desquamation, and raw bleeding lesions on the legs. The right ear was discharging. The liver was large and firm, but the spleen was not palpable. No other abnormalities were detected. The Hb was 5.5 g.%, red cells 1,950,000 per c.mm., haematocrit 19%, reticulocytes 2.9%, leucocytes 16,500 per c.mm. The blood film showed many macrocytes, some microcytes, but only occasional poikilocytes (mean corpuscular diameter

7.42 μ, standard deviation 1.3 μ, macrocytosis 15%, microcytosis 4.2%—see Fig. 1). Fifteen normoblasts and macronormoblasts and one intermediate megaloblast were seen per 100 white cells, which included one large metamyelocyte. Iliac marrow showed normoblasts, some basophilic megaloblasts, many large haemoglobinized erythroblasts with lobed nuclei, and giant metamyelocytes. Abnormalities were absent in the urine and stool, although the latter was oily. Plasma proteins were 3.5 g.%, albumin 1.5 g.%, bilirubin 0.4 mg. per 100 ml. On admission there were no abnormal chest signs, but *x*-ray examination on the following day showed bronchopneumonic infiltration in the right upper lobe with an associated pleural effusion, detectable clinically on the next day. This appears to have been a terminal bronchopneumonia, for the child died shortly afterwards. Permission for necropsy was refused.

Discussion

Kwashiorkor is a syndrome due to protein deficiency in the diet, and it might be expected that the anaemia accompanying it has the same cause, as Altmann and Murray have suggested. Cartwright (1947) has reviewed the evidence that protein deficiency produces anaemia in animals, while Keys *et al.* (1950) have shown experimentally in man that anaemia develops during starvation. In prisoner-of-war and concentration camps anaemia was often associated with low plasma proteins following starvation (Vaughan *et al.*, 1945; Leyton, 1946; Mollison, 1946; Walters *et al.*, 1947), but it was not established that this was a primary protein-deficiency anaemia. Leyton demonstrated a relationship beween the plasma protein level and haemoglobin, but Mollison was not able to show a similar correlation. He considered anaemia to be due to lowered metabolism and not to any specific deficiency.

It is difficult to assess the role of protein deficiency in the production of anaemia in kwashiorkor. Often in severe cases anaemia is mild, and there is no correlation between the haemoglobin on admission and the plasma proteins in this series of cases (see Fig. 4). It has been seen that there is often a drop in haemoglobin and haematocrit levels while oedema is decreasing and plasma proteins are increasing, which appears to exclude protein deficiency as the cause of anaemia. These changes, however, can probably be explained by variations in blood volume. In his oedematous cases at Belsen, Mollison found the blood volume to be lowered, but in other studies of hunger oedema there are conflicting reports (Denz, 1947). On indirect evidence in these oedematous cases of kwashiorkor, it seems likely that the blood volume is initially low and that it rises as soon as plasma proteins increase. As a result the blood count appears to drop. In no case has there been evidence of haemolysis or blood loss, and the changes in blood counts were often so rapid that they could be explained only by changes in blood volume. Under these circumstances the reticulocyte count, which is independent of changes in blood volume, will be a better index of response to treatment than haemoglobin or haematocrit levels. In most cases treated with high-protein diets only there have been small early rises in the reticulocyte count. Similar small rises were observed by Altmann and Murray. It is thus possible that some factor present in soured milk (maas) has stimulated erythropoiesis; but other factors such as increased metabolism might be responsible, and no definite conclusion can be drawn regarding the effect of protein replacement on blood production.

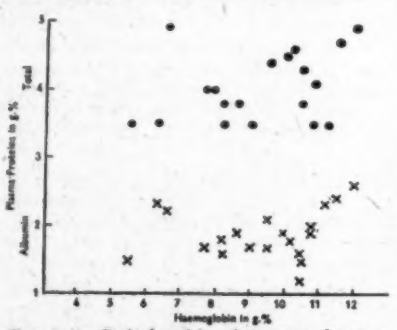

FIG. 4.—Relationship between haemoglobin on admission and total plasma proteins (●), and between haemoglobin and plasma albumin (×).

In Nigeria, Woodruff (1951) describes the predominant anaemia in pregnant African women living on protein-deficient diets as macronormoblastic and seldom megaloblastic. He showed by liver biopsy that the liver is diffusely fibrosed in many cases, and in others infiltrated with fat, and he believes that the similarity to kwashiorkor extends to the anaemia. Both may be due to underlying chronic liver disease, which is known to be accompanied by macronormoblastic erythropoiesis (Bodley Scott, 1939). Woodruff's bone-marrow findings are certainly similar to those described in this paper, but the two anaemias differ in some respects. It is perhaps worthy of note that, contrary to his experience in West Africa, severe megaloblastic anaemia of pregnancy, responding to folic acid and sometimes to vitamin B_{12}, is not uncommon among African and Indian women in Durban, many of whom live on diets low in protein.

In infancy, megaloblastic anaemia has been reported by Zuelzer and Ogden (1946), who described 25 cases. Zuelzer *et al.* (1947) carried out serial studies of the bone marrow in patients with infantile megaloblastic anaemia. They showed that there are patterns varying from predominantly normoblastic to frankly megaloblastic marrow pictures, and in all they record satisfactory responses to folic acid. Zuelzer and Ogden believe that nutritional deficiencies are partly responsible for the production of megaloblastic anaemia in infancy, and it would be surprising if nutritional megaloblastic anaemia were not sometimes encountered in a severe nutritional syndrome like kwashiorkor.

In the cases presented here it has been seen that megaloblastic transformation of the marrow occurs, although it is unusual. Dacie and White (1949) have described megaloblasts in the bone marrow of mild cases of Addisonian pernicious anaemia, the degree of deviation from normal being closely linked with the severity of the lack of haemopoietic factors. In East Africa, Foy *et al.* (1952) have described two groups of macrocytic or normocytic anaemia. In one there are giant stab cells in the bone marrow with erythroblasts, macronormoblasts, and megaloblasts in various stages of development; in the other giant metamyelocytes are present without megaloblasts. Both respond to haemopoietic substances. In kwashiorkor there is also a group in which the marrow contains giant metamyelocytes and some cells which are intermediate between normoblasts and megaloblasts. In two of these there have been satisfactory responses to crude liver extract or to vitamin B_{12}, so it would appear that these cases are examples of developing stages of nutritional megaloblastic anaemia.

There are also similarities between this marrow picture and the type of bone-marrow change in idiopathic steatorrhoea reported by Cooke *et al.* (1948). In kwashiorkor, Thompson and Trowell (1952) have demonstrated a deficiency of pancreatic enzyme production. Some of the stools examined in this series were microscopically oily, but clinically they were neither bulky nor fatty. Subclinical fat-absorption defects, with associated anaemia, however, have not been excluded, since fat-balance studies in African infants are technically difficult to perform.

In the detection of this type of anaemia in kwashiorkor examination of the blood alone for macrocytosis is of little help. Non-megaloblastic macrocytic anaemias occur in a variety of conditions. When appreciable anaemia is found on admission, or when it develops as oedema disappears, the bone marrow should be examined, and in those cases with megaloblastic change—partial or complete—liver extract, vitamin B_{12}, or folic acid should be administered in addition to high-protein diets.

Summary

In a series of 21 cases of kwashiorkor, selected only on the presence of pitting oedema, dermatosis, and lowered plasma proteins, appreciable normocytic or macrocytic anaemia was found in six cases, while two-thirds of the children had less than 9 g.% haemoglobin.

Anaemia may increase considerably as oedema decreases and plasma proteins rise. In this way severe anaemia may be unmasked.

Megaloblastic change was present in two cases. In six others there were bone-marrow abnormalities consisting of giant metamyelocytes and scanty red-cell precursors of intermediate type. Two of these had satisfactory haematological responses to crude liver extract or to vitamin B_{12}.

The possible relationship of this anaemia to protein deficiency, liver disease, and nutritional megaloblastic anaemia is discussed.

I thank Dr. Pauline Klenerman for giving me full access to her cases of kwashiorkor in African children, Dr. N. A. Rossiter for facilities to study Indian children under his care, and Dr. J. Parker, medical superintendent, for permission to publish these cases. Thanks are also due to Dr. J. Thomas, Director of Pathological Services, and his staff for their help with the biochemical estimations; and to Dr. Joan Scragg and the sisters for their assistance.

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The Minister of Education has issued a circular (272, 1954) about the precautions necessary to avoid food poisoning in the preparation and service of meals in school canteens. One of the objects of the Food and Drugs Amendment Bill at present before Parliament is to secure better hygienic conditions in places where food is prepared or served. The prevention of the contamination of food served in canteens depends, however, in large measure on the constant vigilance and the observance of hygienic practices by the canteen staffs. The Minister emphasizes that the risks of food poisoning are present wherever meals are prepared and served, and that there is no reason whatever to think that school canteens are more exposed to them than other forms of corporate meals. After briefly describing some typical examples of outbreaks of food poisoning in school canteens, the circular goes on to consider the prevention of food poisoning in schools under the following headings: Co-operation between medical, teaching, and kitchen staff; health of food handlers; hygienic conditions in the kitchen; the preparation and cooking of food; domestic animals and pests; milk supply; and notification of outbreaks of food poisoning to the medical officer of health. Under the last heading it is recommended that authorities should take steps to ensure that any outbreak of food poisoning is notified immediately, preferably by telephone, to the borough or district medical officer of health, so that he can begin his investigations and take precautionary measures without delay.

ADRENOCORTICAL FUNCTION IN BURNED PATIENTS

WITH SPECIAL REFERENCE TO A.C.T.H. AND ADRENALINE TESTS

BY

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This paper is concerned with the activity of the adrenal cortex of burned patients, and in particular with a search for evidence of adrenocortical failure arising during the illness. The investigation is based on the spontaneous changes in the blood eosinophil count in burned patients, on the changes in the circulating eosinophils induced by injection of pituitary adrenocorticotrophic hormone (A.C.T.H.) or adrenaline, and on other findings.

In a previous paper (Sevitt, 1951) it was shown that a definite pattern of changes affects the number of blood eosinophils after burning (Fig. 1). Within a few hours their number is found either to be falling or to have fallen to low or zero values. This eosinopenia, which is accompanied by a neutrophil leucocytosis and commonly by some lymphopenia, is maintained for a variable number of days, after which the count begins to rise, to reach a peak value within the next few days. Evidence was produced which indicates that the eosinopenia after burning is a sensitive reflection of adrenocortical hyperactivity. This pattern of changes has been confirmed by Evans and Butterfield (1951) and by Wight *et al.* (1953).

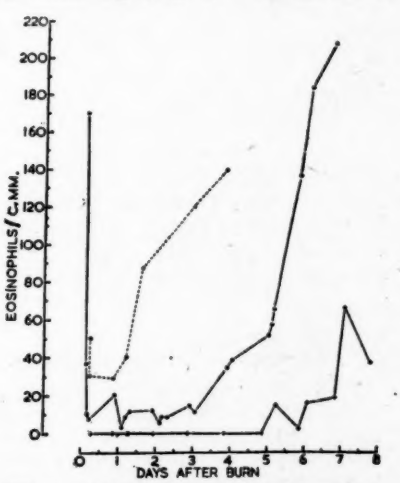

FIG. 1.—Serial blood eosinophil counts during the first week after burning in three patients. In one patient the falling of the count soon after burning is seen, and this is followed by a period of eosinopenia, which is present in all three. The eosinopenia lasted 1, 5, and 7 days respectively in the three patients and was followed by a rise in the count.

The *period of eosinopenia* during which eosinophils are few or absent in the blood stream is maintained for varying periods in different patients and is terminated by the *post-eosinopenic rise* (Fig. 1). The duration of the periods of eosinopenia was estimated in 35 patients with an accuracy within $\pm\frac{1}{4}$ day. In Fig. 2 these periods are plotted against the skin area burned, which is expressed as a percentage of the total skin area. In patients with burns covering less than 10% of the body area the periods of eosinopenia are only one or two days, but are longer, usually three to five days, in those more extensively burned. The relationship between the eosinopenic period and the percentage area seems to be an exponential zone with its concavity facing to the left, rising steeply between four and six days after burning.

Several points, however, fall away from the correlation zone. On clinical evidence it was concluded that in those patients with a more prolonged period of eosinopenia—for example, Case 22—the percentage area burned underestimated the degree and duration of shock and stress. On the other hand, a period of eosinopenia appreciably shorter than that "expected" from the area burned may be due to one of three causes. Firstly, stress after burning may be less than expected

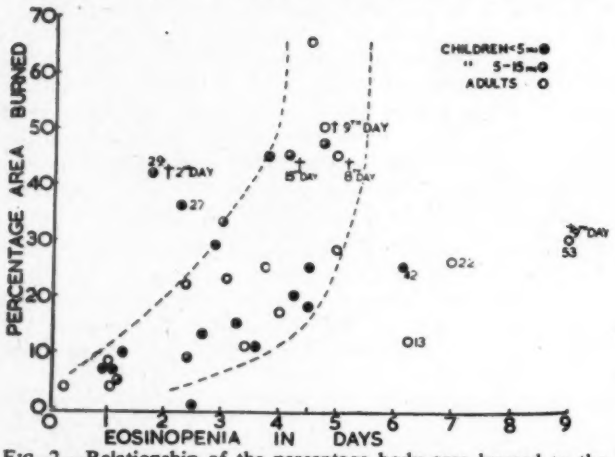

FIG. 2.—Relationship of the percentage body area burned to the duration of eosinopenia in 35 patients (see text). †=died. The numerals are case numbers.

from the area burned, and this may be reflected in physiological abatement of adrenocortical activity (Case 27); secondly, the eosinophils may become resistant to the action of adrenal steroids; and, thirdly, adrenocortical failure may be suspected (Case 29, see below).

Eosinophil Changes in Those Fatally Burned

Eighteen patients were investigated, including the eight previously reported (Sevitt, 1951). Eleven died during the period of eosinopenia, including one who died four hours after burning whilst the eosinophil count was falling. It is concluded that these patients died with hyperactive adrenal cortices. Their ages varied from 1½ to 77 years (five were younger than 12 years, four older than 75 years), nine were females, and the extent of body areas burned ranged from 30% to 80% in the different patients.

In the other seven patients post-burn eosinopenia was not present at the time of death (see Table). In two of them (Cases 29 and 30) adrenocortical failure may have occurred.

In Case 29, which was reported previously, there was a zero eosinopenia for only 1¾ days after burning, indicating adrenocortical hyperactivity during this period. After this a sudden hyperpyrexia and a rapid deterioration of the patient took place. At the same time the eosinophils returned "prematurely" to the blood stream and the patient died a few hours later. Biochemical changes in the heart blood removed immediately after death were consistent with acute adrenocortical failure, but previous oliguria complicated the picture. Case 30 is discussed later.

In the remaining five patients (see Table) there was no evidence of adrenocortical failure. One patient (Case 28) died three hours after burning without a fall in the eosinophils, but eosinopenia may have occurred had he lived long enough. Two (Cases 32 and 36) died a few days after normal periods of post-burn eosinopenia, and these indicated that adrenocortical hyperactivity was present at least for the duration of the eosinopenia. In Cases 44 and 49 the normal A.C.T.H. or adrenaline tests five and seven days before death (15 and 10 days respectively after burning) indicated normal stimulable reserves of the adrenal cortex at the time of the tests.

Stimulation of the Adrenal Cortex by A.C.T.H. and Adrenaline

An injection of A.C.T.H. or cortisone in normal persons produces a significant fall in the blood eosinophil count, but in patients with Addison's disease cortisone, but not A.C.T.H., produces this effect (Thorn *et al.*, 1947; Dougherty and White, 1947; Forsham *et al.*, 1948; Hills *et al.*, 1948; Prunty, 1950). A.C.T.H. therefore does not act directly on the peripheral organs, but its action is mediated through an increased glyco-corticoid secretion from the adrenal cortex.

The secretion of A.C.T.H. by the anterior pituitary is under hypothalamic control probably via an endocrine secreted by the hypothalamus into the hypophysial portal blood supply (de Groot and Harris, 1950; Hume and Wittenstein, 1950). Hume and Wittenstein also showed that this hypothalamic-adrenocorticotrophic activity can be produced by nervous stimuli from an injured area and that this activation occurs through the spinal cord. This is obviously of significance in burns.

Intravenous adrenaline produces an increase of adrenocortical activity (Vogt, 1944), but this does not occur in the hypophysectomized animal (Long and Fry, 1945). From this and other work we may conclude that a *small* dose of adrenaline has little or no direct effect on the adrenal cortex, although this is not necessarily true of large doses, and that adrenaline produces its major effect on the adrenal cortex indirectly through the pituitary gland (Harris, 1951). The site of action of adrenaline is uncertain. It may be the adenohypophysis itself (McDermott *et al.*, 1950), but, if not, it is above this level, possibly in the hypothalamus. In future discussion the site of action of adrenaline will be referred to as the hypothalamic-pituitary or supra-adrenal level.

Seven Patients in Whom the Post-burn Eosinopenia Was Not Present at the Time of Death

Case No.	Sex and Age (Years)	Surface Area Burned	Interval Between Burning and Death	*Eosinophils	A.C.T.H. and Adrenaline Tests	Conclusion
29	F 9	42%	1¾ days	Post-burn zero eosinopenia rising to 11, 99, and 127 a few hours before death ("premature" rise)		Adrenocortical hyperactivity after burning, possibly followed by adrenocortical failure
30	F 5½	49%	15 ,,	Post-burn eosinopenia 4½ days. Ante-mortem eosinopenia	A.C.T.H. test on 5th day=rise of 26%	Adrenocortical hyperactivity after burning and before death, ? temporary period of adrenocortical failure
28	M 80	40%	3 hours	257, 276, 268, at 1½, 2, and 2½ hours		None
32	F 36	50%	9 days	Post-burn eosinopenia 4¾ days		Hyperactive adrenal cortices a few days before death
36	F 38	45%	8 ,,	Post-burn eosinopenia 5 days		
44	M 9	25%	20 ,,		Normal adrenaline test 15th day.	Normal functional reserves of adrenal cortices at times of death
49	F 2½	30%	17 ,,		Normal A.C.T.H. tests 8th and 10th days	

* Hours and days refer to period since burning: other numerals are eosinophils per c.mm. of blood.

A.C.T.H. and Adrenaline Tests on Burned Patients

If a lesion is present in the adrenal glands—for example, bilateral destruction by haemorrhage—neither A.C.T.H. nor adrenaline will depress the eosinophil count.

If a recent lesion is present at the hypothalamic-pituitary level in a patient with intact adrenal glands, an injection of a small amount of adrenaline will have no effect on the adrenal cortex and the eosinophil count will not fall. On the other hand, injected A.C.T.H. will stimulate the adrenal cortex and the eosinophil count will fall. Failure of adrenaline to lower the eosinophil count could reflect a disturbance at the supra-adrenal level: conversely, if an adequate eosinopenia is produced by a small dose of adrenaline the hypothalamic-pituitary adrenocortical mechanism may be considered intact.

A.C.T.H. and adrenaline tests were therefore performed on burned patients. The 21 patients tested were among the more severely burned and were all "shock" cases transfused with plasma or dextran. Twenty had burns involving 20% or more of the body surface, eight 30% or more.

The other factors involved in the interpretation of results are considered later.

Techniques of the Tests

One or two eosinophil counts on capillary blood were made one to 30 minutes before the injection, after which the counts were repeated hourly for four to six hours. The eosinophil counts were plotted against time after injection and the maximum *change* in the count was expressed as a percentage of the pre-injection level: a fall was given a negative value—for example, −60%—and a rise a positive value—for example, +15%.

The *B.P.* solution of adrenaline, 1 in 1,000, was used and 0.3 ml. (≡0.3 mg.) was injected subcutaneously or intramuscularly.

The A.C.T.H. used (batch numbers J 16205, 27111, 27511, and 28112) was first shown to have the expected eosinopenic activity in normal adults and children. In five of the nine children tested the amount injected was 10 to 12.5 mg., in the remainder of the 14 patients tested 20 to 25 mg. was used.

It was not possible to standardize strictly the times of injection, but in two-thirds of the tests the drug was injected between 10 and 11 a.m., and in most of the remainder before 1 p.m. Abnormal results were repeated when possible.

Eosinophil counts were made by the direct "wet-field" method of Dunger (1910), using the eosin-acetone-water diluting fluid. The blood was diluted 1 in 20 in two pipettes and the cells in 0.65 c.mm. were enumerated in four Fuchs–Rosenthal fields.

Normal Eosinophil Response to A.C.T.H.

In normal people the blood eosinophils fall within an hour or so of injection and continue to fall during the next two to four hours, reaching their minimum level about three to five (usually four) hours after the injection (Fig. 3). Forsham *et al.* (1948), Prunty (1949), and others have shown that an injection of 25 mg. of A.C.T.H. produces an eosinophil depression of 50% or more, usually 60 to 90% four hours after injection, and this has been our experience.

Care was taken in interpreting results because it was thought that the blood level of eosinophils after the injection of A.C.T.H. or adrenaline could be influenced by factors unrelated to the injection. The first of these is the pre-ejection level of the eosinophil count. If this is already low, adrenocortical hyperactivity may already be present, little or no additional activity may be produced by the injection, and a significant eosinopenia may not occur. Secondly, since some of the tests were performed during the post-eosinopenic rise of the eosinophil count, this spontaneous elevating effect might have antagonized the eosinophil-depressing effect of A.C.T.H. or adrenaline. Thirdly, in the diurnal variation of the blood eosinophils there is a morning fall in the count up to about 12 noon, after which the count rises. Therefore, in interpreting the present results, not only the maximum percentage fall in the count and the shape of the curve were considered, but also the possible influence of the above factors.

Normal results were obtained in 12 of the 14 tests with A.C.T.H., the eosinophils falling by 60% to 87% in 11 of them (Fig. 4), and in the twelfth a nearly normal fall of 46% was found. This is not considered significant, as four days later the response to adrenaline was normal. In all but three of the patients the tests were performed 10 days or less from the time of burning and one to five days from the end of the eosinopenic period — that is, during or soon after the post-eosinopenic rise.

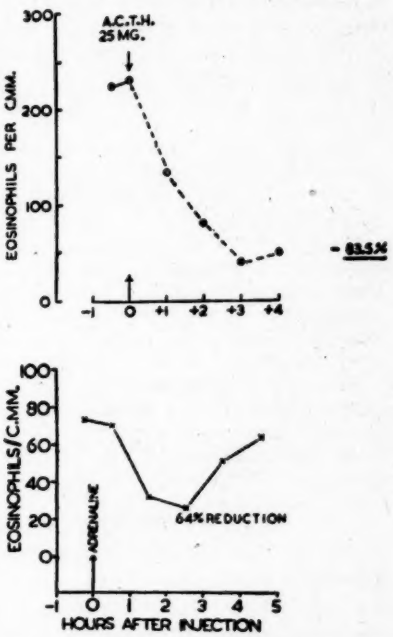

FIG. 3.—Blood eosinophil responses following injections of A.C.T.H. and adrenaline in normal persons. Note that the eosinopenic response to 25 mg. of A.C.T.H. is quicker and more prolonged than that following the injection of 0.3 mg. of adrenaline.

Therefore, in these 12 patients, including one who died a week later, there was no evidence of adrenocortical failure of adrenal gland origin. Three of them, however, showed abnormal eosinophil reactions to adrenaline (see below).

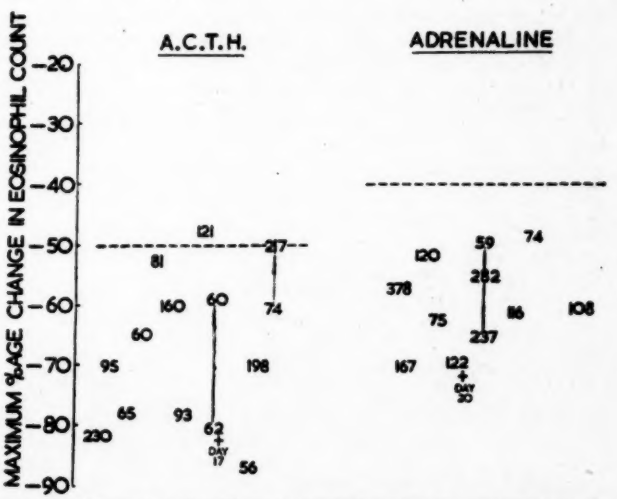

FIG. 4.—Normal A.C.T.H. and adrenaline tests in severely burned patients. Each point is the result of one test. It is represented by a numeral which is the pre-injection value of the blood eosinophil count per c.mm. Its vertical position expresses the maximum percentage lowering of the count. The interrupted horizontal lines at −50% for A.C.T.H. and −40% for adrenaline represent the upper limits considered to be normal. The dotted vertical lines join the results of two or more tests on one patient. Fourteen of the A.C.T.H. tests were normal. These were done on 12 patients, one of whom subsequently died. Eleven of the adrenaline tests were normal, and these were done on nine patients, one of whom subsequently died. + = died.

Normal Eosinophil Response to Adrenaline

In normal people the shape of the eosinophil curve following adrenaline (Fig. 3) differs from the response to A.C.T.H. Usually little or no fall in the eosinophil count is found at an hour after injection; thereafter the count falls to reach its lowest level at two to three hours, and at four hours the count may be rising again. The adrenaline effect is usually slower and shorter than the effect of A.C.T.H. The maximum fall in the count varies between 45% and 70%.

Here it will be assumed that a lowering of the blood eosinophil count to 40% or more of the pre-injection level is normal, provided that the shape of the curve is within normal limits.

Normal curves were found in 9 patients (11 tests: Fig. 4) of the 12 patients tested, with maximum eosinophil depressions ranging from 47 to 70% (average 61%). Eight were tested within 15 days of burning, one of whom died from duodenal obstruction 20 days after burning and five days after the adrenaline test. Subsequent tests on one patient were also normal, as were the responses to A.C.T.H. in two others. Therefore, in these nine patients there was no evidence of adrenocortical failure. Indeed, the results indicated a normal function of the supra-adrenal adrenocortical pathway.

Abnormal Response to A.C.T.H.

Two of the 12 patients tested responded abnormally and one subsequently died.

Case 30

A girl of 5½ years, having burns involving 49% of the body area, was admitted shocked and with haemoconcentrations six hours after burning. She received 6 litres of intravenous plasma and 300 ml. of blood. Attacks of hyperpyrexia occurred on the first and ninth days after burning and slight jaundice on the fourth day. Her burns became colonized with *Ps. pyocyanea.*

Eosinopenia was present on admission and lasted just over four days, indicating hyperactivity of the adrenal cortex during this period. On the fifth day, during the post-eosinopenic rise of the eosinophil count, 12.5 mg. of A.C.T.H. was injected, but the eosinophil count never fell. Instead it rose from 108 per c.mm. before injection to a maximum level of 135 (+26%) at four hours after the injection (Fig. 5). Her blood pressure was normal (120/80) and normal blood glucose values (120 to 140 mg. per 100 ml.) were found. She became anaemic and was transfused. Her condition worsened, *eosinopenia reappeared* on the ninth day (eosinophils 12 per c.mm.), and was maintained until her death 15 days after burning, zero values being found during the last three days.

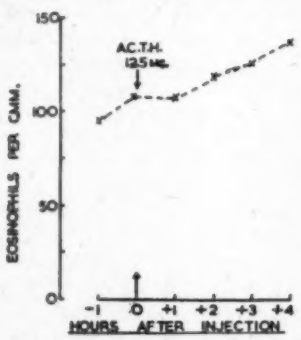

FIG. 5.—Case 30. Abnormal blood eosinophil reaction to an injection of 12.5 mg. of A.C.T.H. The eosinophil count does not fall after the injection, suggesting that adrenocortical failure is present.

At necropsy, purulent bronchitis was found. The *adrenals* were swollen and congested; histologically very little cortical lipoid remained and small foci of haemorrhage were present. Such changes are common in fatally burned patients, particularly in children who die during the period of eosinopenia, and are largely due to intense adrenocortical hyperactivity (unpublished observations). However, many of the columns of the zona fasciculata were transformed into pseudo-acinous or pseudo-tubular structures by an albuminous exudate containing occasional polymorphs. These changes were noted by Rich (1944) in diphtheria and in meningococcal and other infections, and he suggested that they may explain the circulatory collapse. The lymph nodes of the lymph glands, tonsils, and the spleen showed central degenerative changes with oedema, cytoplasmic swelling, and rupture. These changes, which are commonly found after burning (Bardeen, 1898; Baker, 1945), also occur after the injection of A.C.T.H. and are probably due to adrenocortical steroids.

The abnormal response to the A.C.T.H. test during life and the pseudo-acinous degeneration of the adrenal cortex found at necropsy support a diagnosis of adrenocortical failure. However, the reappearance of eosinopenia on the ninth day after burning and the degeneration of lymphoid tissue found at necropsy do not support this view. If adrenocortical failure occurred it was a temporary phenomenon.

Case 52

A 6-year-old girl with burns involving 45% of her body was admitted shocked and with haemoconcentration one and a half hours after burning. She was transfused with dextran, plasma, and blood. Eosinopenia was found, and lasted three and a half days, indicating early adrenocortical hyperactivity. On the fifth day after burning, at the peak of the post-eosinopenic increase of eosinophils, 20 mg. of A.C.T.H. was injected. An unusual curve was obtained: the eosinophils did not fall from the pre-injection level of 287 per c.mm. for two and a half hours after the injection; at three and a half hours the count was falling sharply to a maximum depression of 49% at four hours, but at five hours the eosinophils had increased to more than their pre-injection level. Three days later the test was repeated, and this time the count rose hourly for five hours from the pre-injection level of 152 per c.mm. On the following (ninth) day a test showed a curve of nearly normal shape though the maximum fall was only 39%, but on the sixteenth day a normal curve was found (−73%). Biochemical investigations on the eighth and ninth days gave normal values for blood glucose (120 mg. per 100 ml.) and serum chloride (595 mg. per 100 ml.), but the serum sodium (285 mg. per 100 ml.) and the serum potassium (15.1 mg. per 100 ml.) were slightly low. On the seventeenth day the child excreted 1.2 mg. of 17-ketosteroids in the urine, probably normal for her age (King, 1951).

Clinically the child was never very seriously ill and she made a good recovery. If the abnormal eosinophil responses to A.C.T.H. on the fifth and eighth days indicate adrenocortical failure, then this was of short duration and of no clinical significance. On the other hand, the four A.C.T.H. injections may have excited a therapeutic effect.

Abnormal Responses to Adrenaline

Results of tests were abnormal in three patients, each of whom responded normally to A.C.T.H. Two were children in whom the abnormal responses were associated with a temporary abnormal mental state. When the children recovered mentally the adrenaline responses were found to be normal.

Case 31

A girl of 8 years with burns involving 47% of the body surface was admitted shocked and with haemoconcentration two hours after burning. Her transfusion with 6.2 litres of plasma and 1 litre of blood was probably excessive, as a temporary attack of pulmonary oedema occurred soon after. She became pyrexial —100–102° F. (37.8–38.9° C.). Meanwhile post-burn eosinopenia was found, and lasted 4.7 days. Her mental state and behaviour at this time became abnormal. She was confused, irritable, and querulous. Six days after burning, at the peak of the post-eosinopenic rise of the eosinophils, adrenaline failed to lower the eosinophil count significantly (−12%) (Fig. 6). This was confirmed two days later (−4%), and again on the 38th day after burning (−11%), although on the 15th day an A.C.T.H. injection produced a normal eosinophil response. Gradually,

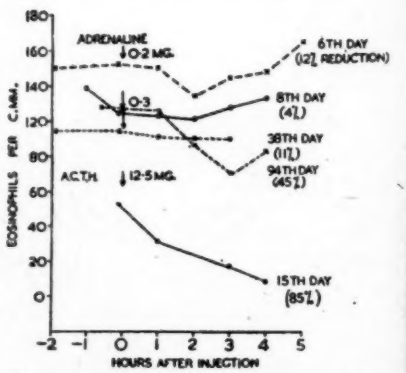

FIG. 6.—Case 31. Abnormal blood eosinophil responses to adrenaline occurred on the 6th, 8th, and 38th days after burning, when little or no change in the eosinophil counts followed the injections. However, the response to the A.C.T.H. test on the 15th day was normal. During this time the child was mentally abnormal. An adrenaline test was normal on the 94th day, when the child's mental condition had returned to normal.

with careful nursing and feeding, blood transfusion, and successful skin cover by grafting, the child improved. Three months after burning, when she had once again become a likeable, normal, and intelligent child, an injection of adrenaline produced a normal eosinophil-depression curve (−45%).

Case 43

A girl of 9 years with burns involving 33% of the body area was admitted one and a half hours after burning, shocked and with haemoconcentration. She was transfused with 6 litres of plasma in the first 24 hours: a short-lived oliguria and oedema of unburned areas occurred. Meanwhile the patient had become delirious and irrational (? cerebral oedema). Eosinopenia was found, and lasted three days. On the sixth day after burning, and at the peak of the rising eosinophil curve, the eosinophil response to A.C.T.H. was normal, but two days later an injection of adrenaline failed to lower the eosinophil count (Fig. 7). At 14 days, when her mental condition was improving, adrenaline depressed the eosinophil count by 40% —"borderline" normal result. Within a month of burning she was behaving naturally and was mentally normal. Four months after burning an adrenaline test produced a normal eosinophil depression curve (−77%).

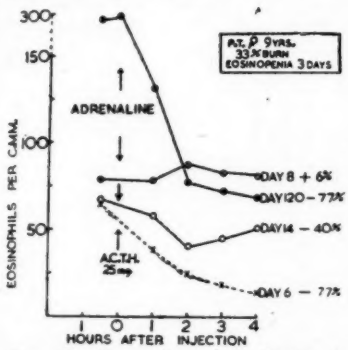

FIG. 7.—Case 43. An abnormal blood eosinophil response to adrenaline (+6%) occurred on the 8th day after burning, although the A.C.T.H. test was normal two days before. During this time the child was mentally abnormal. On the 14th day her mental condition was improving and a "borderline" normal result of −40% was found after adrenaline. Four months after burning, when she was again mentally normal, the eosinophil depression curve to adrenaline was normal (−77%).

The third patient with an abnormal response to adrenaline was a man in whom the A.C.T.H. response was normal. Clinically there were no unusual features, and it was not found possible to repeat the test.

Discussion

In a previous paper it was concluded that adrenocortical hyperactivity always occurs after significant burning (Sevitt, 1951). This was confirmed and extended in the present study, the main aim of which was to determine whether physiological failure of the adrenal cortex occurs in some patients. This was considered important, since "replacement" therapy with A.C.T.H. or cortisone may be indicated.

In 5 of the 54 patients studied there was evidence suggestive of adrenocortical failure. In one patient the evidence was based largely on a "premature" return of the blood eosinophils after a relatively short post-burn eosinopenia associated with clinical deterioration and, soon after, the death of the patient. In the absence of a post-mortem examination the evidence could not be conclusive. In two patients the eosinophil responses to A.C.T.H. were abnormal. One of them was not unduly ill, and the initial abnormal reactions to A.C.T.H. found within 10 days of burning were succeeded by a normal test a week later. In the other patient the abnormal reaction to A.C.T.H. and the pseudo-acinous change in the adrenal cortex found at necropsy support a diagnosis of adrenocortical failure, but the development of an ante-mortem eosinopenia and the finding of degenerative changes in the lymphoid tissue at necropsy indicate that the patient died with hyperactive adrenal cortices. If adrenocortical failure occurred in these two patients it was no more than a temporary phenomenon.

Nevertheless, two of these three patients died. The prognosis of severely burned patients with a tentative diagnosis of adrenocortical failure, based either on a premature rise in the eosinophil count or on an abnormal eosinophil response to A.C.T.H., may be very serious. Therefore, in spite of the uncertainty whether or not adrenocortical failure occurred or was of clinical significance, it is suggested that such patients should be treated with cortisone as soon as the tentative evidence of adrenocortical failure is obtained.

Two children showed abnormal eosinophil reactions to adrenaline, associated with disturbed mental states: the reactions became normal when the mental conditions of the patients were either improving or had returned to normal. This association may be more than a coincidence. The cerebral changes may have involved not only the higher centres to produce mental disturbance but the lower centres, including the hypothalamic area or its central connexions, and so have interfered with the site of action of adrenaline. With recovery of the brain, adrenaline would again become eosinopenic. On the other hand, adrenaline tests performed on a child with a "true" encephalitis developing during the burn illness gave a normal result. Treatment with A.C.T.H. may be indicated in these patients.

Summary

A study of adrenocortical activity was made in 54 burned patients. It was largely based on the spontaneous changes in the eosinophil count found after burning, and, in 21 of the patients, upon the changes induced by a test dose of A.C.T.H. or adrenaline.

It is concluded that adrenocortical hyperactivity always occurs after significant burning. In 49 out of the 54 patients there was no evidence of subsequent adrenocortical failure, and these included 16 of the 18 patients who died.

In five patients, two of whom died, there was evidence of adrenocortical failure. In one a "premature" rise in the eosinophil count after burning was associated with clinical deterioration, and death soon occurred.

Twelve of the 14 patients tested with A.C.T.H. gave normal eosinophil depression curves, indicating normal stimulable reserves of the adrenal cortex. However, eosinopenia was not induced in a young girl tested on the fifth day after burning, suggesting that adrenocortical failure was present; but the spontaneous eosinopenia developing a few days later indicated that, if failure had occurred earlier, it was of short duration. She died 15 days after burning. In another child, not unduly ill, several abnormal reactions to A.C.T.H. were found within 10 days of burning, but on the sixteenth day the test was normal. She survived.

In nine out of twelve patients tested with adrenaline, normal eosinophil depression curves were obtained. The abnormal results found in two children indicated adrenocortical failure at the hypothalamic-pituitary level, since the A.C.T.H. tests were normal. The children were confused and irrational at the times of the abnormal reactions, but later, when normal adrenaline reactions were found, mental recovery had taken or was taking place. It is suggested that both the mental disturbance after burning and the persistence of circulating eosinophils after adrenaline were due to similar changes affecting the cerebral cortex and hypothalamus respectively.

I am in part-time employment of the Medical Research Council. The A.C.T.H. was made by Armour Laboratories and was obtained through the courtesy of the allocation committee of the Medical Research Council. Thanks are due to Messrs. R. Gill and C. Richardson, of the photographic department of the hospital, for photographing the figures, to various members of the

laboratory staff for help with the eosinophil counts, and to Miss M. Hayes. Finally, the co-operation of Sister M. Nicholls and other members of the nursing staff is gratefully acknowledged.

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THE ACHLORHYDRIC PATIENT WITH DYSPEPSIA

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Among those patients who are referred to hospital with a complaint of dyspepsia there remain after routine investigation an appreciable number in whom no satisfactory diagnosis is reached despite the fact that they give the impression of having organic disease. Such cases are usually labelled functional or nervous dyspepsia, or, if there is no free hydrochloric acid secreted in response to a test meal, achlorhydric dyspepsia. Gastroscopic examination will provide a satisfactory explanation of the symptoms in a large proportion of cases. Not only may small ulcers and ulcer scars which have been missed at a barium meal *x*-ray examination be discovered by this means, but it is also the most satisfactory method of confirming the presence of and differentiating gastritis. Where gastritis is found it is, however, impossible to give a reliable prognosis regarding the future comfort of the patient or to assess the possibilities of complications such as bleeding, ulceration, or the development of gastric carcinoma. As many patients have gastritic changes without dyspepsia it is also impossible to be dogmatic on how much the patients' symptoms are attributable to the gastric condition.

Schindler (1947) has given a good working classification of chronic gastritis. He divides cases into four types—hypertrophic, superficial, and atrophic gastritis, and gastritis in the post-operative stomach.

Chronic hypertrophic gastritis seems to be a very rare condition in this country and is not to be confused with the simple hypertrophy with thick folds and prominent areae gastricae which is a normal variant and is the usual finding in patients with hyperchlorhydria and duodenal ulcer. In hypertrophic gastritis intramucosal scarring has led to unevenness of the mucosal pattern, and there may even be pseudo-polypoid changes.

In chronic superficial gastritis there is uneven congestion of the mucosa and excess adherent mucus. Simple diffuse reddening of the mucosa is a physiological state, whereas a stippled or variegated appearance is pathological. Non-adherent mucus is a normal exudate and mucopus is usually swallowed sputum.

The atrophic group is characterized by thinning of the gastric folds, inability to distinguish the areae gastricae, and, when atrophy is marked, by the ability to see the intramucosal and submucosal vessels through the thinned mucosa (Fig. 1). There is often an element of inflammation, shown by congestion along the tips of the folds and by stippling of the mucosa. The appearance of gastric atrophy may be generalized or patchy, and a localized variety is not infrequently seen in the vicinity of ulcer scars. This latter is in reality a new thin mucosa or a stretched mucosa around a scar (Fig. 2).

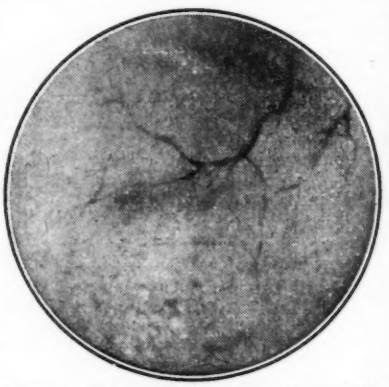

FIG. 1.—Gastroscopic view of atrophic gastritis, showing visible submucosal vessels.

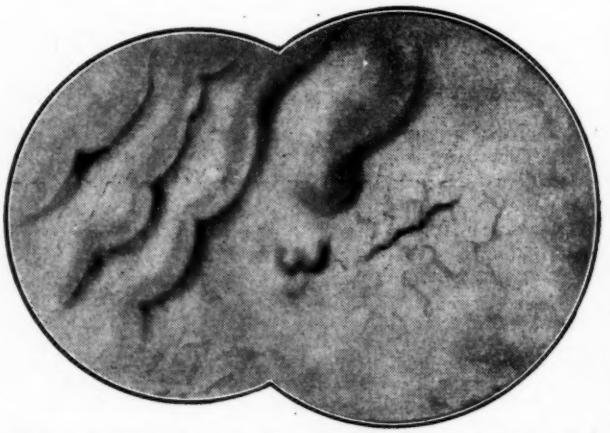

FIG. 2.—Gastroscopic view, showing atrophic gastritis with vessels more prominent in the vicinity of a healed gastric ulcer. Either a true adenoma is present or there is pseudo-polypoid change as a result of scarring. The folds towards the greater curve are normal.

Present Investigation

The case summaries of all patients attending the Gastro-enterological Clinic, St. James's Hospital, London, during the years 1940–6 inclusive have been studied. Where a finding of achlorhydria on a first fractional test meal using gruel as the stimulant was recorded and where some address for the patient was given, the case reports have been abstracted. Certain groups have been followed up during 1952, giving minimum and maximum observation periods of five and twelve years.

These patients are almost without exception those with gastro-intestinal symptoms. It is well known that the

absence of free hydrochloric acid need not produce symptoms. It occurs in a proportion of otherwise normal people, it is an invariable accompaniment of pernicious anaemia, and is common in such diverse conditions as rheumatoid arthritis, steatorrhoea, and various chronic skin diseases.

The records of 403 patients with achlorhydria have been found, and these have been grouped as follows :

Carcinoma of the stomach	63
Pernicious anaemia	15
Advanced atrophy without pernicious anaemia	113
Superficial gastritis and early atrophy	126
Chronic duodenal ulcer	13
Normal gastroscopy—no other cause found	21
No gastroscopy—no other cause found	52

These figures give no true indication of the incidence of the different conditions. Superficial gastritis and early atrophy are not necessarily associated with achlorhydria. Gruel is a comparatively weak stimulant, and had it been combined with an injection of histamine some cases would certainly have secreted hydrochloric acid. In some cases the finding was either false or only temporary. Thus, in the duodenal ulcer group, although the majority had pyloric stenosis with retention gastritis, there were some in whom the tube was evidently not in the stomach. Such cases can usually be eliminated, as no starch can be found in any sample of the gastric aspiration. In the present series, however, we have not been able to exclude them, since a number were referred from other hospitals merely for gastroscopy, and no detailed reports of the analysis are available.

Some of the groups can be disposed of rapidly. Active duodenal ulcers are never associated with achlorhydria, except when complicated by retention gastritis. In this paper we are not concerned with those patients who presented initially with a gastric carcinoma, and this group is not analysed.

The gastroscopic appearances of patients with pernicious anaemia are identical with those of atrophic gastritis. Weighty evidence suggesting that pernicious anaemia is a precursor of gastric carcinoma has been advanced by Kaplan and Rigler (1945, 1947) and Rigler, Kaplan, and Fink (1945), but confirmation of their conclusions must be awaited, since Wilkinson (1945), in a series of 1,600 patients with pernicious anaemia, was unable to find any such association. In the present series there are only 15 patients. The majority did not have gastric symptoms. Nine are still alive, four are dead (one from gastric carcinoma two and a half years after gastroscopic discovery of atrophic changes), and the remaining two have not been traced.

The bulk of the paper is devoted to the superficial gastritis, the early atrophic, and the advanced atrophic groups associated with achlorhydria. The remaining two—those with normal gastroscopic findings and those in whom no gastroscopy was performed—are referred to only where they have something of interest to offer.

Superficial Gastritis; Gastric Atrophy

Patients with advanced atrophy are easily separated from the remainder by reason of the presence of visible submucosal vessels on gastroscopy. In the case of chronic superficial gastritis and early atrophy, however, there seems to be no sharp dividing line, and, at any rate in the presence of achlorhydria, the two conditions overlap. For this reason no attempt has been made to separate them, and they are referred to hereafter as the early atrophic group. A further complication in analysing these patients is that at any stage acute gastric erosions, acute, subacute, or chronic gastric ulcers, or old ulcer scars may occur. The presence of these alters the clinical findings to some extent, and it will often be necessary to separate the cases from their parent groups. There are a few cases of chronic gastric ulcer with achlorhydria in which the gastric mucosa was reported on as normal. Their inclusion in this analysis should not affect the results, as the chronic gastric ulcer cases are dealt with separately where they depart from the general run of the findings. Patients in whom the only evidence of advanced atrophic changes was in the vicinity of ulcer scars are placed in the early group.

The Atrophic Groups

The data concerning the age and sex of the patients are outlined in Table I.

TABLE I.—*Atrophic Gastritis—Age and Sex Incidence*

Age Group	Early Atrophy			Advanced Atrophy		
	Men	Women	Total as %	Men	Women	Total as %
Under 30	1	5	4·8	—	3	2·7
30–	13	3	12·7	8	3	9·7
40–	13	11	19·0	11	9	17·7
50–	20	17	29·4	21	18	34·5
60–	17	11	22·2	19	14	29·2
70–79	6	7	10·3	4	2	5·3
Unknown	1	1	1·6	1	—	0·9
Total	71	55		64	49	

The ratio of men to women is about four to three in each group of the patients, but further division (Table II) suggests that this inequality may be due to the inclusion of patients with gastric ulcers.

TABLE II.—*Atrophic Gastritis—Sex Incidence*

	Early Atrophy		Advanced Atrophy		Combined	
	Men	Women	Men	Women	Men	Women
Acute erosions	7	10	6	13	13	23
Acute ulcers	6	3	6	3	12	6
Subacute ,,	1	2	2	1	3	3
Chronic ,,	27	7	7	4	34	11
Ulcer scars	9	9	4	2	13	11
Remainder	21	24	39	26	60	50
Total	71	55	64	49	135	104

The acute-erosions group has been taken to include not only cases in which an erosion was actually seen, but also those with manifest haemorrhage in which no lesion other than gastritis was found. Table II shows that these erosions were nearly twice as common in women as in men, while chronic gastric ulcers were three times more common in men than in women. If the erosion cases are kept with their parent groups and the ulcer cases are not included there is no great difference in the sex incidence.

The age distribution in the various subgroups is approximately the same, the highest incidence being in the fifties. As can be seen from Table I, there is a wide distribution, the youngest patient in the advanced atrophy group being a 17-year-old girl and the oldest a 79-year-old man. If the population at risk is taken into account there is probably an increasing incidence with increasing age.

TABLE III.—*Atrophic Gastritis—Age at Onset of Symptoms*

Age Group	Ulcers + Atrophy	Remainder	
		Early Atrophy	Advanced Atrophy
10–	1 (1·2%)	1 (1·7%)	4 (5·4%)
20–	9 (10·8%)	4 (6·9%)	6 (8·1%)
30–	15 (18·1%)	13 (22·4%)	15 (20·3%)
40–	26 (31·3%)	11 (19·0%)	14 (18·9%)
50–	21 (25·3%)	14 (24·1%)	20 (27·0%)
60–	9 (10·8%)	11 (19·0%)	10 (13·5%)
70–79	2 (2·4%)	4 (6·9%)	5 (6·8%)
Total	83	58	74

Patients in whom the age at onset was unknown have been omitted.

The onset of symptoms is commonest between the ages of 30 and 60, with a maximum incidence in the fifties (Table III). There is little difference between the early and late groups. Where there is a concomitant ulcer the distri-

bution resembles more closely that of chronic gastric ulcer, with a maximum incidence in the forties.

The data concerning the length of history of symptoms are set out in Table IV, where it has been necessary to subdivide the groups. A greater number of patients with

TABLE IV.—*Atrophic Gastritis—Length of History of Symptoms*

Length of History (Years)	Combined Groups				Remainder	
	Erosions	Acute and Subacute Ulcers	Chronic Ulcers	Scars	Early	Advanced
Under 1 ..	13 (38·2)	9 (39·1)	11 (28·2)	6 (28·6)	16 (38·1)	17 (30·4)
1– ..	8 (23·5)	4 (17·4)	12 (30·8)	7 (33·3)	14 (33·3)	12 (21·4)
5– ..	4 (11·8)	3 (13·0)	2 (5·1)	1 (4·8)	6 (14·3)	10 (17·9)
10– ..	5 (14·7)	4 (17·4)	8 (20·5)	6 (28·6)	5 (11·9)	8 (14·3)
Over 20 ..	4 (11·8)	3 (13·0)	6 (15·4)	1 (4·8)	1 (2·4)	9 (16·1)
Total ..	34	23	39	21	42	56

Patients in whom the length of history was unknown have been omitted.

early atrophy present with a short history of symptoms than do those with advanced atrophy. This is not unexpected, since atrophy is presumably a progressive process. Indeed, it is probable that gastritis is a degenerative rather than a true inflammatory condition. However, nearly a third of those with advanced atrophy have a history of under one year's duration. Possibly some added factor such as inflammation, an exogenous irritant, or a transitory erosive process is required for the production of symptoms.

It has been suggested that the low acid values associated with chronic gastric ulcer are secondary to the presence of the ulcer. Table IV suggests that this is not necessarily so. In a series of 498 patients with chronic gastric ulcers previously analysed, about 40% gave a history of symptoms of under five years' duration, while in the present series the figure is 60%. This increase is explained by the inclusion of patients who were found at other hospitals to have a short history of symptoms combined with achlorhydria and an ulcer crater, and who were referred here for gastroscopic examination to exclude malignancy. This does not interfere with the finding that low acid values in chronic gastric ulcer are often associated with a long history of ulcer symptoms, and we again stress that chronic gastric ulcer is in most cases probably the outcome of degenerative changes in the gastric mucosa (Tanner, 1951).

Symptomatology of the Atrophic Groups

Epigastric Pain and Discomfort

Over 90% of patients complained of epigastric pain or discomfort, the most common form being pain related to meals (Table V).

TABLE V.—*Chronic Gastritis—Pain Related to Meals*

	Pain Related to Meals	Remainder
Early atrophy, including erosions ..	37 (59·7%)	25 (40·3%)
Late " " " ..	47 (56·0%)	37 (44·0%)
Acute and subacute ulcers	14 (58·3%)	10 (41·7%)
Chronic ulcers	36 (81·8%)	8 (18·2%)
Ulcer scars	10 (43·5%)	13 (56·5%)

Patients in whom the symptomatology was unknown are not included.

The erosion cases have been kept with their parent group. If they are separated the findings are not materially altered. The patients with chronic gastric ulcer are more likely to complain of post-prandial pain than the remainder, but of those without a demonstrable break in the continuity of the gastric mucosa over half complain of this symptom. The mode of production of the pain is intriguing and obscure. It appears to differ little from that accompanying peptic ulceration, though in the late atrophic group it seems to come on more often directly after eating. This is not always so, but the details of the time relationship to meals are insufficient for statistical analysis.

In some patients the pain is relieved by alkalis (it is well known that many achlorhydric dyspeptics complain of "acidity"). In some cases vomiting, and in others taking food, gives relief; some find that nothing helps. Relief from taking food follows the general rule that the longer the interval between eating and the onset of pain the more likely is food to afford relief.

Comparatively few patients in whom ulcer scars in addition to atrophy were found complained of post-prandial pain, since these patients not infrequently present with manifest haemorrhage without a previous history of dyspepsia.

Only 8% of patients with chronic ulcers (compared with 18% in the early atrophic and 25% in the late atrophic groups) complained of pain unrelated to meals.

The symptoms of fullness or discomfort after meals were rarely prominent in the chronic ulcer patients, but were present in 18% of the early atrophic and 15% of the late atrophic parent groups.

Manifest Haemorrhage

It has been found in this clinic that 50% of patients with haematemesis or melaena in whom no gross cause is found for the bleeding have gastroscopic evidence of atrophic changes (Tanner, 1949). The data in the present series are set out in Table VI.

TABLE VI.—*Chronic Gastritis—Manifest Haemorrhage*

	History of Haemorrhage	No History of Haemorrhage
Early atrophy, including erosions ..	17 (27·4%)	45 (72·6%)
Late " " " ..	18 (21·4%)	66 (78·6%)
Acute and subacute ulcers	13 (54·2%)	11 (45·8%)
Chronic ulcers	11 (25·0%)	33 (75·0%)
Ulcer scars	10 (43·5%)	13 (56·5%)

TABLE VII.—*Haemorrhage*

	Haemorrhage with Preceding Dyspepsia	Haemorrhage as Sole Symptom
Early atrophy, including erosions ..	13	4
Late " " " ..	14	4
Acute and subacute ulcers	11	2
Chronic ulcers	11	—
Ulcer scars	6	4

There is a history of haemorrhage in about a quarter of the cases of early and late atrophy, but when these are complicated by acute or subacute ulcers or ulcer scars the figure is doubled (Table VI). The incidence where there is an additional chronic ulcer is not higher than for the parent groups, and is approximately the same as in patients with chronic ulcers without achlorhydria (Swynnerton and Tanner, 1953).

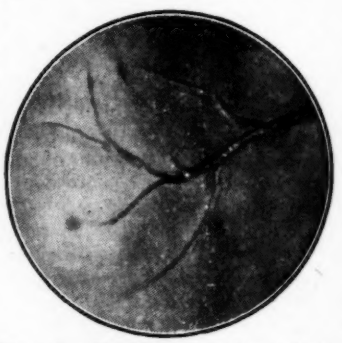

FIG. 3.—Gastroscopic view of an acute erosion, overlying a visible submucosal vessel.

In an appreciable number of cases haemorrhage may be the only symptom (Table VII).

In some cases an obvious lesion may be found from which the bleeding comes, but in others there may be no obvious bleeding point even in those rare cases which continue to bleed and come to necropsy. However, one of us has seen acute erosions overlying visible submucosal vessels (Tanner, 1949), and it may be that these patients are more

susceptible to mucosal erosion than normal and a shallow erosion into a submucous vessel may cause copious haemorrhage (Fig. 3).

Other Symptoms

Nausea, Vomiting, Anorexia, Weight Loss.—The symptoms of nausea and vomiting, anorexia, or weight loss are present in approximately a fifth of the patients (Table VIII).

TABLE VIII.—*Nausea and Vomiting, Anorexia, Weight Loss*

	Nausea and Vomiting	Anorexia	Weight Loss
Early atrophy, including erosions	12 (19·4%)	11 (17·7%)	14 (22·6%)
Late " "	16 (19·0%)	13 (15·5%)	19 (22·6%)
Acute and subacute ulcers ..	2 (8·3%)	4 (16·7%)	7 (29·2%)
Chronic ulcers	6 (13·6%)	6 (13·6%)	10 (22·7%)
Ulcer scars	1 (4·3%)	5 (21·7%)	6 (26·1%)

Note: The totals on which percentages are based may be obtained by reference to Tables V or VI.

The presence of an ulcer does not greatly affect the incidence except in the case of nausea and vomiting, which is less frequent when an ulcer is present. So far as possible those patients who vomited merely in an attempt to relieve their symptoms and those who were afraid to eat have been omitted.

Bowel Habit.—Complaints of diarrhoea or constipation as prominent symptoms were uncommon, the maximum incidence being in the parent late atrophic group, in which one in ten complained of diarrhoea and one in twenty of constipation. Bowel habit is dealt with more fully in the late analysis.

Lassitude and anaemic symptoms were complained of by less than one in ten of the patients. Other more uncommon main complaints included belching, regurgitation, and dysphagia.

Conclusions on Symptomatology

Over 90% of the patients complained of epigastric pain or discomfort, most often related to meals. One in five was troubled with vomiting, anorexia, or weight loss; and one in three had manifest haemorrhage at some stage during the course of the disease. To sum up, there is no definite clinical picture to distinguish chronic atrophic gastritis from peptic ulceration or gastric carcinoma, and it may at times mimic gall-bladder disease, hiatus hernia, or many other disorders.

Associated Conditions

Gastric Adenomata.—In five of the 113 patients with advanced atrophy there were coexistent gastric adenomata—in two a single adenoma was seen; in one there were two adenomata, and in two the adenomata were multiple. In the early atrophic group one woman had two adenomata, and in one man a doubtful adenoma was seen at a later date.

Gall-bladder Diseases.—Six of the 113 patients in the advanced atrophic and 7 of the 126 in the early atrophic groups had a past, concurrent, or subsequent history of gall-bladder disease. Since the two conditions may be indistinguishable clinically, mistakes concerning the causation of symptoms are bound to occur. Thus patients who have had a cholecystectomy may return to hospital with their symptoms unaltered, while others in whom both conditions are found at the same admission may be permanently relieved by cholecystectomy. It is even possible that the dyspeptic symptoms of gall-bladder disease (not, of course, colic) may be due to a coincident gastritis or duodenitis, for it is well known that flatulent dyspepsia may persist after cholecystectomy.

Chronic Respiratory Infections.—Fourteen patients in the late and 10 in the early groups suffered from chronic bronchitis. It is not possible to say whether the two conditions are associated, since chronic bronchitis is a common condition in South London, but an incidence of 10% would seem to be high. Four patients in the late group have been diagnosed as suffering from pulmonary tuberculosis, and another gave a past history of tuberculous peritonitis. In the early atrophic group two gave a history of pulmonary tuberculosis.

Tertiary Syphilis.—Three patients in the late and two in the early groups had tertiary syphilis. Three of these had syphilitic aortitis and the other two had tabes dorsalis. In one of the former, submucous gastric swellings were seen on gastroscopy, and these disappeared after antiluetic treatment.

Other Associated Conditions.—These include psoriasis (2), chronic dermatitis (1), osteoarthritis (3), rheumatoid arthritis (1), haemophilia (1), cysteinuria (1), and diabetes mellitus (1).

Late Results

The method of follow-up of patients was the same as that previously described (Swynnerton and Tanner, 1953). Results are rather less complete than in the follow-up of cases of chronic gastric ulcer, for two reasons: (1) that the records of addresses and next-of-kin were often less detailed; and (2) that four of the patients referred from other hospitals were war refugees from Malta and Gibraltar whom it has proved impossible to trace. The general results of the follow-up investigation are given in Table IX.

TABLE IX.—*Atrophic Gastritis—General Results of Follow-up*

	Early Atrophy	Late Atrophy
Alive—adequate information ..	78 (61·9%)	82 (72·6%)
" —inadequate " ..	2 (1·6%)	1 (0·9%)
Dead	38 (30·2%)	22 (19·5%)
No information	8 (6·3%)	8 (7·1%)
Total	126	113

Deaths

The causes of death in the early and late atrophic groups, in those with a gastroscopically normal mucosa, and in those in whom no gastroscopy was performed are shown in Table X.

TABLE X.—*Causes of Death*

	Late Atrophy	Early Atrophy	Normal Mucosa	No Gastroscopy
Gastro-intestinal:				
Gastric carcinoma	—	3	—	1
" ulcer	—	2	—	—
" haemorrhage ..	1	—	2	—
Carcinoma of large bowel ..	1	1	—	1
Sarcoma of ileum	—	—	—	1
Carcinoma of gall-bladder ..	—	2	—	—
" " pancreas ..	—	—	1	—
Appendicitis	—	1	—	—
Mediastinitis	—	1	—	—
Cardiovascular:				
Heart failure	7	13	2	3
Syphilis	1	1	1	—
Cerebral vascular accidents ..	3	2	1	1
Respiratory:				
Chronic bronchitis	—	3	2	1
Acute infections	2	2	—	—
Tuberculosis	4	2	1	1
Carcinoma of bronchus ..	1	1	—	—
Renal:				
Pyelonephritis	1	1	—	1
Chronic nephritis	—	—	—	1
Other:				
Aplastic anaemia	—	—	1	—
Accidents	—	1	—	—
Suicide	1	—	—	—
Unknown	—	2	—	2
Total	22	38	11	13

The figures in the early atrophic group again draw attention to the fact that the dyspepsia may be due to causes other than the gastritis, and one should not be satisfied with a single diagnosis of chronic gastritis before excluding all other possibilities. Thus the two patients with carcinoma of the gall-bladder both died less than two months after gastritis had been found. It would seem possible, too,

that in a number of those dying of "heart failure" the achlorhydria and gastroscopic appearances may have been secondary to chronic cardiac disease.

The average age at death in the advanced atrophic group was 67.6 years, only two patients having died under the age of 60—one of tuberculosis and the other of syphilitic aortitis. Of those patients still alive at least one is over 90. In the early atrophic group the average age at death was 65.

In the advanced atrophic group, apart from the one patient who died of uncontrolled gastric haemorrhage, no patient appears to have died either as a direct or as an indirect result of atrophy.

Carcinoma of Stomach

In the late atrophic group none of the traced patients have developed a gastric carcinoma and only two of them have developed a malignant tumour elsewhere in the body. In some 3% of all people the cause of death is attributed to gastric carcinoma (Registrar-General, 1953), so it is reasonable to suppose that if atrophic gastritis is a precursor of gastric carcinoma one might find a certain number of cases in the present series. The essentially negative findings are in line with the only other series of gastroscopically confirmed cases found in the literature. Findley *et al.* (1950) followed for five years or more 100 patients, of whom 49 had "mild," 33 "moderate," and 18 "pronounced" atrophy, and found none who developed gastric carcinoma.

In the early atrophic group four patients have developed gastric carcinoma and seven a carcinoma elsewhere in the body. The former are analysed further :

Case 1.—A man aged 52 was admitted on December 5, 1941, with an eighteen-months history of epigastric pain immediately after meals. Fractional test meal analysis showed achlorhydria. Gastroscopic examination revealed no gross abnormality apart from fine congestion of the mucosa. Barium-meal examination revealed no lesion. He was reinvestigated in 1943 and 1944 on account of recurrent symptoms. On both occasions a barium-meal examination was normal. In 1943 gastroscopy showed thinning of the mucosa without visible vessels and a small adenoma. This latter was not seen in 1944. He was seen at the follow-up clinic in April, 1952, when he still complained of similar symptoms. On examination a large epigastric mass was palpated. He was admitted and died following removal of a large adeno-carcinoma of the body of the stomach.

Case 2.—A man aged 70 was admitted on February 3, 1942, with a two-years history of epigastric pain two to three hours after meals associated with anorexia and vomiting. Fractional test meal analysis showed achlorhydria. Gastroscopy revealed marked congestion of the mucosa and a chronic gastric ulcer at the angulus. In view of his general condition a gastro-jejunostomy instead of a partial gastrectomy was performed after failure of the ulcer to heal on medical treatment. He continued to have recurrent dyspepsia, and the ulcer was again seen gastroscopically in August, 1944. He was readmitted in May, 1947, when he had an epigastric mass, a palpable irregular liver, and ascites. He died a few days later. Permission for a necropsy was refused.

Case 3.—A woman aged 73 was admitted on February 17, 1945, with a four-years history of vague epigastric pain and recent lassitude. A barium-meal examination showed no lesion. Fractional test meal analysis showed achlorhydria. Gastroscopy revealed a mucosa which was thin in patches and associated with speckled congestion. For technical reasons the examination was incomplete, and it was thought that there might be a lesion at the angulus. She was readmitted in May, 1948, with a six-months history of pallor, lassitude, and anaemic symptoms. There was no further mention of dyspepsia. Severe hypochromic anaemia was found. During her stay in hospital she developed sudden pain in the epigastrium and died on June 9, 1948. At necropsy a small flat carcinoma was found arising ½ in. (1.3 cm.) proximal to the pylorus. In addition there was a subphrenic abscess.

Case 4.—A man aged 51 was admitted on August 25, 1941, with haematemesis preceded by a week of epigastric discomfort after meals. Fractional test meal analysis showed achlorhydria. Barium-meal examination showed an innocent ulcer on the lesser curve and this was confirmed gastroscopically. The gastric mucosa was reported to be otherwise normal. The ulcer was shown to be soundly healed seven weeks later. He returned in May, 1946, with a history of recurrence of dyspepsia for the past year. On gastroscopy the ulcer was thought to be innocent, but at operation and on section it was found to be a diffuse infiltrating spheroidal-cell carcinoma.

Apart from the presence of achlorhydria there is no factor common to these four cases. In three there was mucosal congestion, in two an apparently innocent chronic gastric ulcer, and in two evidence of atrophy of the mucosa. It is not possible to reach any conclusion on the study of these cases.

Pernicious Anaemia

One patient, a 69-year-old man, was diagnosed as suffering from pernicious anaemia three years after the initial gastroscopic diagnosis of advanced atrophy. Two other patients gave family histories of pernicious anaemia.

Late Results in Patients Still Alive

In the advanced atrophic group eight patients have had partial gastrectomies performed—seven for chronic ulcer and one for gastric polyposis—leaving 74 for late assessment. The early atrophic group is loaded with patients with concurrent chronic gastric ulcers, and, since these ulcers are just as apt to recur as those in patients without achlorhydria, it has been decided to omit them from the late analysis. Fifty patients remain alive and were followed up. The subsequent course of events in the two series is shown in Table XI.

TABLE XI.—*Chronic Gastritis—Late Results*

	Early Atrophy Excluding Chronic Ulcers		Late Atrophy		Total	
	No.	%	No.	%	No.	%
No further trouble	13	(26·0)	18	(24·3)	31	(25·0)
Occasional mild symptoms ..	16	(32·0)	21	(28·4)	37	(29·8)
,, severe ,, ..	1	(2·0)	3	(4·1)	4	(3·2)
Frequent or constant symptoms	20	(40·0)	32	(43·2)	52	(41·9)

The results in the two series are very similar. Just over half the patients have had little or no further trouble from their stomach. Chronic superficial gastritis and the earlier stages of atrophy are conditions which may heal completely (Schindler, 1947), and, as we know from patients with pernicious anaemia, advanced atrophy need not cause symptoms.

Nearly all the patients in the advanced and many in the early atrophic group were advised to take a mixture containing hydrochloric acid, but only 11 have continued to do so, while 59 take alkalis more or less regularly.

The reason for this swing from acid to alkalis is threefold. First, patients find hydrochloric acid unpleasant to take, no matter how much diluted or disguised; secondly, dyspepsia means to general practitioners a prescription for alkalis, and the recommendation to prescribe acid is soon forgotten; and, thirdly, many patients find that alkalis are effective for relieving their symptoms. A wide variety of alkalis were used with good effect.

The bowel habits of 39 patients with early atrophy and 59 with advanced atrophy are known (Table XII). Constipation is common in the advanced atrophic group, while diarrhoea, either in attacks or as a constant looseness of the motions, is present in one in ten.

TABLE XII.—*Bowel Habit in Patients with Atrophic Gastritis*

	Early Atrophy	Advanced Atrophy
Normal	22 (56·4%)	24 (40·7%)
Constipation	12 (30·8%)	27 (45·8%)
Diarrhoea	5 (12·8%)	6 (10·2%)
,, or constipation ..	0 (0·0%)	2 (3·4%)

Discussion

The diagnosis of chronic gastritis should be accepted as the cause of the patient's symptoms only after exclusion of all other possible conditions. Confirmation of its presence will be obtained only by gastroscopic examination. Blind biopsy methods such as that described by Wood *et al.* (1949) may help to elucidate the process of gastritic changes, but will be unreliable for diagnosis, as the condition is often patchy.

The prognosis regarding symptoms is somewhat better than in the medical treatment of chronic gastric ulcer, since about half the patients have very little subsequent trouble. Amongst the other half there are a few who become disgruntled, finding that different regimes of treatment have little effect on their symptoms. A dietary regime similar to that used in patients with chronic gastric ulcer should be followed, and during exacerbations bed rest will undoubtedly hasten relief and may be followed by long remissions. A mixture containing hydrochloric acid should be prescribed, to be taken well diluted during meals, and the patient should be allowed to experiment until he finds the most effective flavouring agent, which is most likely to be one of the citrus fruit juices (Bockus, 1944). Hydrochloric acid therapy is usually sufficient to control attacks of achlorhydric diarrhoea, but in obstinate cases it may be supplemented with phthalyl or succinylsulphathiazole. A few patients are of the opinion that acid prevents or terminates attacks of dyspepsia, but this does not appear to be the general finding. If hydrochloric acid is badly tolerated or fails to relieve the symptoms when taken regularly over a period of time, one of the non-absorbable alkalis may be tried, or "autolavage" by taking 1 dr. (4 g.) of sodium bicarbonate in water before meals, as recommended by Spriggs and Marxer (1943).

Supplementary vitamin-B complex is often given to these patients, since there is evidence that a deficiency leads to a decrease in gastric acidity. It has been reported by several observers, notably by Jones, Benedict, and Hampton (1935), that in patients with pernicious anaemia there may be regeneration of the gastric mucosa with liver therapy, but this has been denied by others who regard advanced atrophy as an irreversible state. In this clinic one of us (N. C. T.) has seen a patient with pernicious anaemia whose gastric mucosa showed patchy regeneration on liver therapy. Until there is more evidence on the action of liver extract and vitamin B_{12} on the stomach it would seem to be inadvisable to use them in simple atrophic gastritis for fear of masking the development of pernicious anaemia. Surgery appears to play little part in the treatment of atrophic gastritis. As Schindler (1947) remarks, "there is no reason to believe or to hope that the pain will be alleviated by surgical interference." Patients who have had partial gastrectomies performed for a coexistent ulcer or ulcer scar are not infrequently seen with their symptoms unaltered. In cases of uncontrolled haemorrhage a total gastrectomy would have to be contemplated to guarantee success, since the bleeding areas are often multiple and widely scattered, but in practice a partial resection usually leads to diminution and sometimes to cessation of bleeding.

Opinions concerning the role of chronic gastritis as a precursor of gastric carcinoma have been as much at variance as in the more familiar "ulcer-cancer" controversy. The histological examination of stomachs resected for cancer provides little evidence, for, even if there were general agreement on the degree of gastritic changes, it would still be impossible to decide whether these were the primary condition or whether they were secondary to the presence of the neoplasm. The solution of the problem is therefore a clinical one. The most important work done from the clinical aspect has been that of Comfort and his colleagues (1947) at the Mayo Clinic. They have studied a series of patients with gastric carcinoma who had had gastric analyses performed before the development of the carcinoma. They found that the proportion of low or absent free hydrochloric acid values was greater than normal in these patients, suggesting that carcinoma arises in an already diseased stomach. *It must be borne in mind, however, that this was a selected series of patients, since they were those in whom the carcinoma was preceded by many years of dyspepsia, and it is not possible to estimate the importance of chronic gastric disease in the development of gastric carcinoma as a whole.*

In the present investigation none of the traced patients with advanced atrophic changes have developed gastric cancer. This is negative evidence which is suggestive but by no means conclusive, and, ideally, all these patients should be seen again in another five to ten years. The negative findings are to some extent supported by the sex incidence, which is not that of gastric carcinoma. It is now well established that gastric adenomata are prone to become malignant, and Schindler (1947) has reported that these adenomata are seven times more common in people with gastric atrophy than in those without. The adenomata are presumably secondary to or a variant of the atrophic changes and may form a connecting-link between the atrophy and the development of carcinoma. In the early atrophic series, in which four patients developed gastric carcinoma, it is not possible to estimate whether this is a significant incidence, and the factors involved were multiple. In only two was there macroscopic evidence of atrophy.

It will have been noticed that in 11 of the cases of advanced atrophy there were concomitant chronic benign gastric ulcers. It is usually taught that a diagnosis of gastric ulcer is incompatible with a finding of complete achlorhydria. In some of the present cases the atrophy was patchy, but in others it was generalized, and in these the capacity of the stomach to secrete acid in response to any stimulant must be negligible. It seems probable that hydrochloric acid is essential for the initial formation of the ulcer, but not for its maintenance. This latter may be due to poor healing powers in the degenerate atrophic mucosa and also, possibly, to superadded infection or trauma.

Summary

An analysis and late follow-up has been carried out on a series of patients who were found to secrete no free hydrochloric acid in response to a test meal using gruel as the stimulant. Two main groups of gastroscopically confirmed patients have been dealt with in some detail, the one comprising 113 cases of advanced atrophic gastritis, and the other 126 cases of chronic superficial gastritis or early atrophic gastritis.

The analysis is complicated by the frequent coexistence of gastric erosions or ulcers.

If patients with chronic gastric ulcers are excluded there is no great difference between the incidence in the two sexes.

There is a wide distribution in the age incidence, the majority of patients in the two groups presenting at hospital between the ages of 40 and 70. Information is given on the length of history and age at onset of symptoms.

Over 90% complain of epigastric pain or discomfort, which is usually related to eating.

Over a quarter give a history of manifest haemorrhage, and in one in five of these haemorrhage is the sole symptom. Complaints of nausea, vomiting, anorexia, and weight loss are frequent.

Less common main symptoms include diarrhoea, constipation, anaemia, belching, regurgitation, and dysphagia.

In the advanced atrophic group constipation is four times more common than diarrhoea.

Of associated conditions gall-bladder disease seems to be most important, since it may be clinically indistinguishable from atrophic gastritis, and since there may be direct association between the two. Other associated conditions which may be of aetiological significance include chronic bronchitis, pulmonary tuberculosis, tertiary syphilis, cardiovascular disease, and certain chronic skin and joint conditions.

In the late atrophic group 22 patients (19.5%) have died. In only one, a case of uncontrolled gastric haemorrhage, was there any connexion between the atrophic gastritis and the cause of death. No patient in this group has developed a gastric carcinoma.

In the early atrophic group 38 patients (30.2%) have died. Four of these have developed a gastric carcinoma, but, apart from the absence of free hydrochloric acid, no common factor could be found.

One patient with advanced atrophy was subsequently found to have developed pernicious anaemia.

Among those patients still alive the results in the two groups are very similar. About half have had very little subsequent trouble, but the course of the disease seems to have been little influenced by a variety of regimes in the remainder.

The treatment of atrophic gastritis is discussed.

Some of the evidence concerning the role of chronic gastritis as a precursor of gastric carcinoma is presented, and the apparently anomalous finding of peptic ulcer of the stomach in the absence of free hydrochloric acid is discussed.

We are greatly indebted to the many people, not least the patients themselves, who co-operated in the follow-up. We wish to thank Miss Temple and Mrs. Strong, of the Records Department, St. James's Hospital, and Miss Kirwin for the many hours spent unearthing ancient records, and the latter for her secretarial assistance. The cost of the investigation was met from a grant from the Weir Research Fund.

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The latest issue of *Scientific Film Review* includes appraisals of five medical films. "Coarctation of the Aorta" (E. R. Squibb & Sons), intended for students and society meetings. "Haemolytic Disease of the Newborn" (St. James's Film Unit) depicts the technique of replacement transfusion. "Marrow Puncture" (I.C.I.) surveys the techniques of marrow puncture in patients of various ages. It is intended for housemen and postgraduate students. "Venepuncture" (I.C.I.) demonstrates the technique in adults. These four films are in colour. A black-and-white film mentioned is "Prevention of Infection of Babies in Hospital" (British Film Institute), a comprehensive survey of modes of spread of infection in children's wards. It is for the training of nurses and medical students entering paediatric words. *Scientific Film Review* is published quarterly by the British Film Institute at an annual subscription of 5s.

RESULTS OF TREATMENT OF CHRONIC VASOMOTOR RHINITIS

PART I. RESPONSE TO PHYSICAL TREATMENT

BY

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Sufferers from chronic vasomotor rhinitis form a large proportion of all those attending the throat clinics of most hospitals, and we have been impressed not only by the frequency of the disorder but also by the unsatisfactory response to treatment. In addition it is apparent that many of these patients are emotionally upset, and that their disabilities are in part caused and in part magnified by psychological imbalance.

Results of Physical Investigation and Treatment

A series of 127 consecutive patients were studied. Symptoms, rhinological appearances, allergic responses, and the results of treatment were noted, and a superficial assessment of the emotional background was attempted in the throat clinic (by K. M.). As many as possible were invited to participate in more detailed psychological investigation, and those who did attend may fairly be regarded as a representative sample of sufferers from vasomotor rhinitis.

The main symptom in this disease is either paroxysmal rhinorrhoea or persistent nasal blockage. While well-defined examples of each may be recognized, yet in a great number the two clinical pictures are merged, to give symptoms and signs of both. In this series, there were 46 cases of paroxysmal sneezing and rhinorrhoea and 81 of chronic nasal oedema (49 with polypi and 32 without). A brief recapitulation of the two syndromes is appended.

1. Non-specific Paroxysmal Sneezing and Rhinorrhoea

Sufferers often refer to this as a "constant cold" or hay-fever, because of the similarity of the symptoms.

In non-specific rhinorrhoea the characteristic attacks usually occur in the morning, at or soon after waking; or they may be precipitated by some change in body temperature, as in getting out of bed or walking barefoot on a cold floor, by exposure to bright sunshine, by the inhalation of airborne irritants, especially dust, or by emotional stress. There is a feeling of irritation at the root of the nose, followed by sneezing, lacrimation, and a profuse watery discharge. The rhinorrhoea may last for only a few minutes or may continue for several hours, and as many as 50 large handkerchiefs may be soaked in the course of a day. Nasal obstruction, headaches, and anosmia are not usually features of the condition.

The attacks are distinguished from common colds by the nature of the discharge, which is clear and watery and not purulent as in coryza. Secondary infection can follow these attacks, whereupon the discharge becomes thick and yellow, and the infection is then identical with the later stages of a coryza.

Examination of the nose shows that the mucous membrane has a normal appearance, and during an attack the nasal passages are found flooded with thin mucus. Radiological examination of the sinuses indicates no change beyond a slight and occasional mucosal thickening. Repeated

examination of nasal smears often shows the presence of eosinophils. In this series of 46 cases 15 smears were examined, and 5 were positive—a finding to which no importance is attached.

The response of the skin to tests with allergens is usually non-specific, and we have come to the conclusion that allergy plays little part in the aetiology, as is shown in Table I.

TABLE I.—*Results of* 40 *Skin Tests*

Reaction:	Slight	Moderate	Strong	Total
Negative				12
General non-specific	1	10	5	16
House dust	2	2	3	7
Grass	4	1	0	5

It may be said that people suffering from non-specific rhinorrhoea have a more sensitive nasal mucosa than sufferers from hay-fever; they show brisker nasal reactions to many more irritants and in many more circumstances than do hay-fever subjects, who have been excluded altogether from this analysis.

The symptoms have an explosive character, the counterpart of which in the somatic nervous system would be termed epileptiform. Since the secretomotor nerves of the nose are from the parasympathetic centres in the hypothalamus, such an autonomic "epileptiform attack" would manifest itself in the fashion outlined in the symptoms. Such a concept places the disorder amongst other stress disorders such as asthma and duodenal ulcer, in which the cholinergic system seems to play a leading part.

This hypothesis is in part borne out by the effect of division of the greater superficial petrosal nerve. This nerve is occasionally damaged in fractures of the petrous bone or invaded by new growths, resulting in a "dry nose." From a study of such patients as we have been able to examine in whom this nerve has been injured, it is clear that the greater superficial petrosal nerve is in fact the secretomotor nerve to the nasal mucosa.

For some considerable time a patient has been sought whose rhinorrhoea was so intractable to medical measures and so distressing that any form of relief would be welcomed. When finally such a patient was found, Mr. Murray Falconer performed at our request a section of this nerve through a subtemporal craniotomy. This produced complete homolateral cessation of rhinorrhoea, and the patient is now anxious, after a lapse of six months, to have the other side operated upon. However, our approach must be cautious. The employment of a major surgical operation to rid the patient of what is at the worst a severe discomfort can be justified only if the results can honestly be predicted as completely satisfactory, and if it is reasonably without risk.

Treatment

When the skin tests show no specific reaction or show sensitivity to several allergens, it has proved of little value to attempt hyposensitization or desensitization.

The antihistaminic drugs have been of great value in the control of the rhinorrhoea. To find the particular drug which will prove most effective in any individual nose is a matter of trial and error. It is surprising how often a slight alteration in the radical attached to the ethylenediamine nucleus may make one antihistaminic effective and another useless in the control of symptoms. A combination of antazoline and tripelennamine, such as "dibistin," gives a wider range of control. Results are often gratifying, but treatment must be continuous to correct this persistent disorder, and many patients find daily dosage over months and years very tiresome. That is to say, treatment by these drugs is in no sense treatment of the causes of the disorder, but is merely palliative.

The drowsiness occasioned by antihistaminics can be adequately countered by the administration of amphetamine or dexamphetamine sulphate.

Of the 46 patients suffering from non-specific rhinorrhoea, 32 derived a satisfactory degree of suppression of symptoms from the use of antihistaminics. Two required zinc ionization and have remained symptom-free up to the time of writing (21 months), and three have been relieved for a similar period by specific desensitization (see Table I—three patients with strongly positive reactions to house dust). In five all forms of treatment were completely fruitless.

It may be worthy of remark that some of these patients derive considerable temporary amelioration from the administration of calcium lactate, 10 gr. (0.65 g.) t.d.s., and parathyroid extract, 1/20–1/10 gr. (3.2–6.5 mg.) t.d.s.

2. Persistent Nasal Blockage

This title is used for want of a better term. "Chronic nasal oedema" emphasizes one of the commonest clinical features of the complaint—namely, nasal polypi. These are a frequent cause of nasal blockage in vasomotor rhinitis (Table II).

TABLE II.—*Cause of Obstruction* (81 *Cases*)

	No.	%
Polypi	43	53
Swelling of inferior turbinates	16	20
Polypoidal swelling of middle turbinate	12	15
Mulberry swelling of posterior pole of inferior turbinate	5	6
Deviated septum with vasomotor features	5	6

When the inferior turbinate is swollen the obstruction is due to vascular dilatation under vasomotor influences rather than to extracellular fluid collections. Lucas (1952) has demonstrated the contrast between the filled and closed vascular bed, and one is led to conclude that oedema is not the main factor in this type of obstruction.

Eosinophils may be present in the nasal secretions as in the paroxysmal type of the disease. Of 12 smears taken 6 were positive. The patient refers to his nasal blockage as "catarrh"—"I blow my nose and nothing comes away." Further questions establish that the obstruction affects one or both sides, intermittently or alternately. It is made worse by any interference with the normal mechanism of regulation of the body temperature. For this reason it is worse at night, when the body surface is covered with heavy non-conductive bedclothes. A warm, moist atmosphere makes the obstruction worse. Provided a source of permanent obstruction in the shape of polypi is not present, energetic physical effort in the open air helps to clear the obstruction.

Paroxysmal sneezing and rhinorrhoea may also be present, but generally there is little nasal discharge. A slight postnasal discharge, worse in the morning, is the result of accumulation and drying of the mucus secreted overnight. Frontal, retro-orbital, and occipital headaches are not uncommon, and are caused by temporary blockage of the ostia of the nasal sinuses. Anosmia and "nasal speech" are often reported as a result of the nasal blockage.

Treatment

Chronic nasal obstruction can be alleviated by the rhinologist only by mechanical and, to a lesser extent, by pharmacological methods. The use of the antihistaminics has proved disappointing; their effect on polypi is negligible, and on mucosal swelling slight and inconstant.

Surgical removal of nasal polypi, ablation of the engorged posterior ends of the inferior turbinates, and linear cauterization of the middle turbinates are the measures most commonly employed. Zinc ionization has proved valuable in obtaining long-term freedom from symptoms.

TABLE III.—*Treatment*

Relieved by polypectomy	38
Relieved by cautery of inferior turbinates	16
Relieved by vasoconstrictors	4
„ „ zinc ionization	1
Specific desensitization	2
39 tested: 24 positive, 5 strongly positive	
Antihistaminics, slight relief:	
With polypi	5
Without „	10

As shown in Part II, stress factors influence both clinical groups. When an organic obstruction such as a polyp blocks the nose little change can be expected in the airway under the influence of emotion. On the other hand, one would expect to find a clearer relationship between emotion and the state of the nose when the rhinitis has an episodic character as in paroxysmal sneezing and rhinorrhoea.

Thanks are due to the Board of Governors of Guy's Hospital and to the Research Committee of Guy's Hospital Medical School for the provision of a grant to one of us (K. M.) in the execution of this work.

RESULTS OF TREATMENT OF CHRONIC VASOMOTOR RHINITIS

PART II. RESPONSE TO PSYCHOLOGICAL TREATMENT

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Results of Psychiatric Assessment and Psychotherapy

Thirty-one patients under treatment in the throat and ear department were examined. There are two separate series. The patients in series I (13) were the subjects of a pilot study carried out to discover whether there appeared to be any significant correlation, in general terms, between the emotional life of the patient and variations in nasal symptoms. Those in series II (18) were kept under continuous observation for periods of time varying from 1 to 20 months.

The long-term and short-term behaviour of the illness was reviewed against the background of the patient's day-to-day existence and its vicissitudes. Some attempt was made to deal with emotional tension by psychotherapy in all the patients in series II.

Series I

This series comprised eight women and five men. The age range was 16–66 and the mean age 37.9 years. The patients were interviewed on a few occasions only, and the investigation was on a superficial level. Eight had no other complaints but the rhinitis itself. Case 7 had occasional headaches after an especially laborious task; Case 1 felt sometimes irritable and depressed; and Case 10 was tense and moody. Cases 5 and 8 had multiple symptoms—malaise, "run-down," headache, "indigestion," poor sleep, bad dreams.

When the history of rhinitis was explored by a method which took account of the patient's attitudes, feelings, and reactions to stress, the series could be subdivided into three groups.

Group A.—In four patients no significant association of the symptoms of vasomotor rhinitis with emotional tension could be found. Three of these were placid, stable people who had no mental or physical symptoms of anxiety; nasal function seemed to be influenced by physical agencies, such as change of temperature, but not by emotional state. The fourth was a tense, hostile, paranoid man who showed considerable resistance to a psychiatric approach to his illness. If his resistance and the hostility to which it gave rise had been better handled it might have been possible to demonstrate to him some association of nasal symptoms with feelings, since it was manifest that his feelings were very much disturbed; on the evidence, this association seemed probable but could not be proved.

Group B.—Some relationship between mental state and nasal symptoms was present in eight patients. The emotional states correlated with symptoms in these patients were in the main unpleasant and threatening—anxiety, guilt, resentment, despair. The following case is typical.

Case 10.—A woman of 30 was evacuated from London to the country in 1941. She objected to this move and found her new life dull and tedious; in this setting of frustration and discontent she began to have attacks of sneezing (up to 12 attacks daily, average 12 sneezes each), running of the nose (usually 10 large handkerchiefs daily), and obstruction. Clinically, she had pale swollen inferior turbinates; skin tests were negative. Attacks sometimes followed an argument at work. She was not troubled at all by nasal dysfunction when she was walking out with her boy friend; after he left her she felt disappointed and dejected, and symptoms began again.

Group C.—In one patient rhinitis began at a time of crisis in her life, and its symptoms were plainly related to anxiety. The association between nasal symptoms and emotional tension in this case was thus very close.

The preliminary investigation showed, then, that in only one-third of the series did the nasal disorder bear no relation to stress. Furthermore, it seemed likely that, if some of the patients in group B had been examined more often and a better rapport had been established, other links between the rhinitis and the patient's adjustment might have come to light. It was therefore decided to examine a second series of patients and to keep them under observation long enough to allow variations in the nasal symptoms to be correlated directly with life circumstances and the process of psychotherapy. Information of this kind is more reliable than that taken from the patient's anamnesis.

Series II

This series comprised 11 women and 7 men. The age range was 20–58 and the mean age 35 years. The mean duration of attendance at the out-patient clinic was eight months. During psychotherapy the behaviour of the rhinitis and the patient's attitudes, feelings, and reactions were observed, and the correlation, or lack of correlation, between these was recorded.

Group A

The patient's emotional reaction in three cases was thought to have no influence or an insignificant influence on nasal symptoms. The onset of rhinitis in these patients could not be clearly related to disturbing experiences, and, although there was some association between stress and variations in symptoms, this association did not appear to govern the behaviour of the disorder.

Case 15.—A woman of 48 was left alone when her husband died in 1948. She had few friends and felt isolated from her family. In January, 1951, she caught "flu" and had to stay in bed; she was hurt and disappointed that none of her family came to visit her. Symptoms of rhinitis began after this illness. There did not seem to be any close relation between sneezing and nasal blockage and discharge, and spells of anxiety, tension, and resentment against her family.

Here, although the rhinitis did appear for the first time when the patient was depressed and discontented, it later pursued its own course, apparently uninfluenced by her state of feeling.

Group B

In seven patients emotional tension was one of the main determinants of the illness.

Case 10.—A man of 35 suffered from blocking and running of the nose, "indigestion," and occasional attacks of asthma. The indigestion was very plainly related to anxiety, and some of the asthmatic attacks occurred in a setting of emotional tension. The rhinitis first appeared when he left school and went to work. There were attacks coincident with illness in a relative and in his wife. He experienced a kind of internal agitation when he went to visit his parents: "I feel excited in the stomach." This state was in part pleasurable, but it contained a considerable tension component as well. Three times an attack of rhinitis began at the time of the visit. On the other hand, he had attacks which did

not seem to be related to stress. When the course of the illness was reviewed the attacks associated with emotional tension outweighed the remainder.

Here the stress factor accounted for most of the attacks, but there were others which accompanied a change in climate and some which appeared "out of the blue" for no reason which we could discover. An important association of nasal symptoms in this patient was with relaxation; it was plain from his story that the pathogenic agent was not the relaxation itself but the effort and emotional strain which preceded it. This kind of association is familiar in other stress disorders; it is very often seen in migraine (O'Neill, 1952).

Six of the seven patients had other symptoms besides the rhinitis—anxiety, depression, fatigue, asthma, "indigestion," irregularity of menstruation, and menorrhagia. These may be regarded as mental and physical manifestations of a stress reaction of which the nasal disorder was one component.

The onset of symptoms in five patients occurred at a time of especial difficulty and frustration.

Case 4.—A man of 31 came back to his firm after six years' war service to find that some of his junior colleagues who had not joined up had risen to positions of importance and were now senior to him. "I tried not to be resentful"; but he could not help feeling bitter and indignant. Attacks of sneezing and running of the nose began, and have continued. He observed that annoyance affected the nose: "If my little boy pesters me I sneeze." Nasal symptoms were least in evidence while he was active. "If I mope the nose runs."

Variations in symptoms in these patients could for the most part, though not entirely, be accounted for by their emotional state at the time. This relationship is further discussed below.

Group C

A careful review of the story of the illness in the eight remaining patients led to the conclusion that stress was the dominant factor in the pathogenesis.

Case 6.—Sneezing began in a man of 32 when he was working in a power-station. The work was monotonous and boring, and he felt frustrated: "I want a change. At a loss now. Feel very anxious." In the Army he had risen from the ranks to W.O.1 by diligent application to duty; he was ambitious and believed that he could better himself at work if he had the opportunity. At the same time he was reluctant to resign from the power-station, since the job was secure and carried a pension. While he was under observation every attack of nasal symptoms could be related to anxiety. After several discussions of his attitude to work, and the pros and cons of making a move, he decided to stay where he was, and to accommodate himself to the conditions; he became less restless and more content. When last seen, ten months later, the rhinitis had almost disappeared. There were occasional mild attacks after fits of worry and depression.

A change of attitude and emotional state, brought about by reflection and discussion, was accompanied in this patient by improvement in the rhinitis.

Five of the eight patients had other tension symptoms—fatigue, depression, menorrhagia, "indigestion," bodily pains, and migraine.

In all eight, symptoms of nasal dysfunction began when they were passing through an experience that aroused emotional tension. These experiences, it should be noted, were not in themselves very dramatic or extraordinary. They were disturbing to the patient because of the strong feeling which was mobilized, and their importance depended on the patient's own internal conflicts and not upon disaster in the outside world.

Case 18.—Symptoms (irritation, sneezing up to 30 times, and watery rhinorrhoea for several hours) began in a woman of 29 after she started music lessons with a male teacher. To her, marriage was a symbol of independence, and she ardently desired to form the kind of friendship which might lead to it. Strivings in this direction, however, stirred up anxiety because of a strong bond of dependence on her mother. Beneath this was deeper anxiety; she had once entered into a homosexual relationship of which she was very ashamed, and she was most apprehensive lest her feelings for her own sex should prove stronger than her feelings for men.

Variations in the intensity of nasal symptoms were associated with variations in emotional state in every patient in this group.

Correlation of Nasal Dysfunction with Emotional State

The data for this correlation are taken from observations on all 18 patients in series II. Two types of correlation can be considered: (1) long-term—the association of attacks with painful experiences over the whole course of the illness; and (2) short-term—momentary variation of symptoms with state of feeling, such as the appearance of nasal blockage in a fit of anger. Furthermore, the emotional determination of physical symptoms is often, if not always, a complex process; the immediate apparent precipitant may be found to rest upon other and deeper levels of conflict. Examples of this kind of psycho-physical relationship are given below.

Precipitating Symptoms

The immediate precipitants of symptoms may be classed as follows.

Anxiety from various sources (10 cases) was much the most common. In two of these the chief focus of anxiety was hypochondriacal concern.

Case 8.—Nasal obstruction due to polypi, and watery rhinorrhoea, began in a man of 42 after he had gone to consult a doctor about pain in his side. The doctor told him that he was doing too much and had tachycardia. The patient thought that this meant serious heart disease, and became extremely anxious about himself. He was sent to a cardiologist for an opinion and given strong reassurance. He ceased to worry about his heart, and the rhinitis diminished.

A blend of anxiety and resentment was predominant in three patients, and an association of symptoms with feelings of depression and deprivation was observed in three others. In three patients symptoms would often appear in the phase of relaxation after effort.

In some patients nasal dysfunction tended to be more pronounced in states of fatigue, probably because the power to keep in check painful emotions is lessened at such times.

Sex feeling, in the sense of unsatisfied desire, manifestly contributed to the causation of symptoms in two patients; and in a third (Case 18) conflicts over the sexual role, which gave rise to acute anxiety, came to light over some months through dream analysis. In several patients who were investigated at length, attitudes and feelings which had at first been entirely hidden rose to the surface, and it was then clear that the tension caused by these underlay and reinforced the emotional states which acted as the immediate precipitants of physical symptoms.

Case 1.—A man of 34 took over the editorship of a trade journal in 1946. The journal was a "one-man show," and he was alone responsible for its production and management. He took his work seriously and worried about it. Soon after he started the task he began to notice "repeated colds." He kept a chart of the variation in symptoms, and saw that the nose gave least trouble when he was working efficiently and at high pressure; nasal block and discharge at once appeared when he "flopped" after a period of intense effort. The analysis of dreams led almost at once to the themes of guilt and fear of punishment; then to the association of sex feeling and violence; and then the patient recalled that his first marriage had early come to grief because his wife was frigid. One night, in a kind of fugue state, he had made a furious attack on her. The memory of this experience had been wholly suppressed, and its recall caused him intense distress, and brought into consciousness the fear that he might make a similar attack on his present wife. When the guilt and fear linked with these impulses had been ventilated he was relieved, but said that he thought the primary problem had yet to be reached. The dream thoughts then took up the theme of his relationship to his mother, and the hostility and rebellion which as an only child he felt towards her. In speaking on this theme, strong feeling was expressed, and nasal symptoms gradually diminished until, nine months after his first attendance, the rhinitis ceased to give much trouble.

In this patient the intensity of nasal dysfunction was related to work strain. When the tensions which lay beneath

this had been to some extent alleviated, nasal block and discharge were reduced, though the actual situation at work had not altered.

Effect of Psychotherapy upon Nasal Symptoms

All the patients in series II were treated in the out-patient department by repeated interviews for periods ranging from 1 to 20 months. The sources of tension were explored and the patients were given help to deal with these. Dream analysis was utilized in six cases. The results of treatment were:

	Paroxysmal Rhinorrhoea	Chronic Nasal Oedema
Much improved or recovered	5	3
Improved	3	3
No change	2	1
Improvement in rhinitis, development of asthma	1	—

It will be seen that in response to treatment there was no significant difference between paroxysmal rhinorrhoea and chronic nasal oedema.

The best results were obtained in cases in which the relationship of the illness to stress was strongest, and six of the eight patients in group C were much improved.

These results suggest that sustained improvement in vasomotor rhinitis can be brought about by the diminution in emotional tension which follows psychotherapy—an improvement that does not depend on the use of antihistamine drugs.

Comment

A comparison of the grouping in series I and II shows that the principal difference is in group C (series I, 1; series II, 6). This suggests that the more that is known about the patient, and the better his reactions are understood, the more does the stress factor stand out. This conclusion is confirmed by the clinical findings in those patients who were investigated at greater length. The patient mentioned above (Case 1 of series II) could not, at his first interview, have told of his attack on his wife, since he was not at that time aware of it. The judgment that a particular disorder is not related to stress is a difficult one to make without a really thorough inquiry.

One of the patients in series II (Case 16), who was most anxious and hypochondriacal and suffered from abdominal discomfort, bodily pains, migraine, tension, and depression, had to consult a doctor about his other symptoms; another (Case 3) looked pale and ill, and was depressed and anxious. Both of these patients were manifestly anxious on examination, and their anxiety and its symptoms were severe enough to warrant their seeking medical advice. The other 16 patients did not seem to be very anxious or very depressed, and would not have asked for a psychiatric appraisal if it had not been offered to them. Few of the patients in either series were able, at their first attendance, to relate the symptoms of their rhinitis to stress, yet they were able to grasp this relationship readily enough when it was made clear to them by the anamnesis, and the more intelligent among them strove to make such modifications in their lives as were necessary to keep symptoms to a minimum.

No specific personality pattern emerged from the psychiatric examination of the patients in series II. Reactions of evasion and retreat (Cases 3 and 5) were represented among the patterns of illness, as well as reactions of combativeness and defiance (Cases 10 and 17). Symptoms of nasal dysfunction could appear in anticipation of stress (Case 13), during the stress itself (Case 7), and after it was over (Case 1).

Once the physical symptoms had appeared, utilization of them in order to gain some advantage was not a feature of the illness in any of these patients. In this respect the disorder resembles duodenal ulcer.

Summary

The results of treatment of chronic vasomotor rhinitis by physical and psychiatric methods are reviewed.

A few patients may be relieved of their symptoms by desensitization, and a few more are benefited by zinc ionization. Obstruction of vascular origin, and that due to polypi, can be lessened by cautery and polypectomy. Antihistamine drugs are capable of suppressing the symptoms of paroxysmal rhinorrhoea, but only when they are being given continuously. They do not benefit the patient with chronic nasal oedema.

Some relationship between stress and the onset and course of vasomotor rhinitis has been demonstrated from a superficial psychiatric investigation. When the investigation is more prolonged and is carried to deeper levels a close relationship between nasal symptoms and stress can be shown in most patients. Such a relationship was found in 24 of this series of 31 patients. Recovery or sustained improvement followed psychotherapy in 14 of 18 patients treated at some length.

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COMPLICATIONS OF MECKEL'S DIVERTICULUM

WITH AN ANALYSIS OF 18 CASES

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Meckel's diverticulum has been the subject of many authoritative and stimulating papers in the past. It is not a rare congenital abnormality; the complications of this lesion are, however, of such gravity that the subject is always of importance in any consideration of acute abdominal emergencies. The cases reported here illustrate well some of its more serious complications, and it is by keeping such facts constantly in mind that we may hope to reduce the mortality of such lesions.

The first adequate description was published by J. F. Meckel in a series of three papers which appeared between 1808 and 1815. He was apparently the first to associate the diverticulum with the omphalomesenteric duct which connects the yolk sac with the intestine during the first few weeks of foetal life. Failure of obliteration of part or whole of the duct results in various anatomical types, ranging from complete patency to the outpouching of intestine, usually of the terminal ileum.

Meckel's diverticulum usually arises from the antemesenteric border of the ileum, about 20 in. (50 cm.) proximal to the ileo-caecal valve, the distance being less as the age approaches infancy. The diverticulum is usually composed of the same three layers which make up the ileum, but at times contains heterotopic tissues; the incidence varies between 15 and 25% of cases. It takes the form of gastric, duodenal, jejunal, and colonic mucosa, as well as pancreatic tissue. The most common type of heterotopic tissue is gastric mucosa, occurring in 16.6% of all cases of Meckel's diverticulum. When present, the heterotopic tissue usually lines the greater portion of the diverticulum, often involving the neck of the sac.

Complications

Meckel's diverticulum attracts the attention of the surgeon as a rule only when one of the several complications of this anomaly develop. These include :

1. *Diverticulitis With or Without Perforation.*—Meckel's diverticulum is subject to inflammatory changes giving rise to symptoms and signs similar to those of appendicitis. It is impossible to distinguish between the two conditions with any degree of confidence, unless the patient has had his appendix removed at a previous operation. Perforation with peritonitis may occur, the latter being more lethal than that seen with a perforated appendix, owing to less efficient "walling off" and to greater volume and fluidity of intestinal contents.

2. *Ulceration or Haemorrhage or Both from Heterotopic Gastric Tissue.*—Peptic ulcer with haemorrhage or perforation or both is a common complication of Meckel's diverti-

Summary of Cases

Case No.	Age	Sex	Clinical Features on Admission	Pre-operative Diagnosis	Post-operative Diagnosis	Treatment and End-result
1	21	M	Recurrent severe attacks of melaena extending over period of 10 months requiring transfusion. Barium meal and gastroscopy: N.A.D. History of mild ulcer dyspepsia	? Bleeding duodenal ulcer. ? Bleeding ulcer of Meckel's diverticulum	Bleeding ulcer of Meckel's diverticulum	Simple excision of diverticulum, which appeared to be fibrosed at apex. End-result satisfactory
2	9	M	Admitted with 48-hours history of abdominal pain and vomiting. T. 100·8° F. (38·2° C.). Examination revealed tenderness and rigidity of lower abdomen. Per rectum: tender on right side anteriorly	Acute appendicitis	Gangrenous Meckel's diverculitis	Simple excision of diverticulum. End-result satisfactory
3	39	F	History of colicky abdominal pain and vomiting of 4 hours' duration. T. 99° F. (37·2° C.). Tenderness and guarding high in right iliac fossa and right hypochondrium. Previous but less severe attacks of abdominal pain	Acute appendicitis	Meckel's diverticulitis	Simple excision of diverticulum. End-result satisfactory
4	55	F	Recurrent attacks of melaena associated with vague attacks of upper abdominal pain. Barium meal, barium enema, and gastroscopy normal	Bleeding duodenal ulcer	Bleeding ulcer of Meckel's diverticulum	Simple excision of diverticulum with invagination of the stump. Histology: no heterotopic gastric mucosa
5	33	F	Lower right abdominal pain associated with vomiting for 3 days. T. 98·4° F. (36·9° C.). Also previous attacks of colicky right lower abdominal pain with vomiting for 3 years	Acute appendicitis	Meckel's diverticulitis	Simple excision of diverticulum. Discharged well 2 weeks after operation. Histology suggests heterotopic gastric mucosa
6	9	M	Severe recurrent attacks of melaena necessitating blood transfusion. Barium meal: N.A.D.	Bleeding ulcer of Meckel's diverticulum	Bleeding ulcer of Meckel's diverticulum	Simple excision of diverticulum. Discharged well 7 weeks after operation
7	54	F	Lower abdominal pain and vomiting for 3 days. Rheumatic heart disease associated with fibrillation. On examination there was evidence of slight abdominal distension	Intestinal obstruction		Patient died from toxaemia without any operative intervention. Necropsy showed gangrenous Meckel's diverticulum causing intestinal obstruction
8	38	M	Colicky lower abdominal pain and vomiting	Intestinal obstruction	Meckel's diverticulitis causing intestinal obstruction	Simple excision of diverticulum. As the diverticulum was kinking small intestine and causing marked obstruction, temporary ileostomy was performed. Discharged well about 7 weeks after operation
9	10/12	M	Colicky abdominal pain and vomiting, associated with bleeding per rectum. T. 100° F. (37·8° C.). ? Mass felt in right hypochondrium	Intussusception	Intussusception caused by Meckel's diverticulum	Simple excision of diverticulum. Discharged well 8 days after operation
10	17	M	4 months' history of vague dyspepsia with recent severe attack of melaena requiring blood transfusion	? Bleeding peptic ulcer of Meckel's diverticulum. ? Bleeding D.U.	Bleeding ulcer of Meckel's diverticulum	Simple excision of Meckel's diverticulum. Histology showed heterotopic gastric mucosa. Discharged well 12 days after operation
11	38	M	Intermittent mild abdominal pain for 9 days. Much more severe 24 hours before admission, associated with vomiting. Examination showed tenderness and guarding in right iliac fossa	Acute appendicitis	Gangrenous Meckel's diverticulitis	Excision of diverticulum, plus adjacent portion of small bowel. Discharged well about 4 weeks after operation
12	10/12	M	Painless melaena for one day. Irritability, especially after feeds for a few days. No abnormality found on examination of abdomen	? Intussusception. ? Bleeding ulcer of Meckel's diverticulum	Bleeding ulcer of Meckel's diverticulum	Excision of diverticulum. Discharged well 8 days after operation
13	29	M	2 days' history of colicky mid-abdominal pain. Examination revealed tenderness and guarding in right iliac fossa. T. 102° F. (38·9° C.)	Acute appendicitis. ? Meckel's diverticulitis	Meckel's diverticulitis	Simple diverticulectomy. Discharged well 11 days after admission
14	50	M	5 days' history of abdominal pain and vomiting. On examination no definite distension seen but obstructive sounds heard on auscultation	Intestinal obstruction	Meckel's diverticulum causing obstruction of small bowel	Excision of diverticulum plus adjacent portion of small intestine
15	33	F	20 years' history of pain ½-hour after meals with recent attacks of colicky abdominal pain. One attack of right-sided abdominal pain diagnosed as appendicitis; appendicectomy performed but appendix normal. Meckel's diverticulum was not looked for. Barium meal and gastroscopy negative. Occult blood positive on several occasions	? Ulcer of Meckel's diverticulum	Meckel's diverticulum with ulcer on adjacent portion of small bowel	Excision of diverticulum plus portion of small intestine on each side. The ulcer in this case was in the ileum, 1 cm. proximal to stoma of Meckel's diverticulum. The ulcer had caused ring stricture of small intestine, producing marked intestinal obstruction
16	45	M	2 days' history of generalized abdominal pain and vomiting; pain more marked in right iliac fossa on day of admission. On examination marked tenderness and guarding in right iliac fossa	Acute appendicitis	Gangrenous Meckel's diverticulitis and subacute appendicitis	Simple excision of diverticulum. The diverticulum was divided into two portions by a constriction in its wall, and the larger pouch contained a number of hard stones
17	18	M	2 years' history of occasional dyspepsia. Recurrent attacks of fairly severe melaena extending over a period of 8 months. On examination tender to right of umbilicus. Barium meal normal	? Meckel's diverticulum. ? Duodenal ulcer	Meckel's diverticulum	Simple excision of diverticulum. Post-operative progress satisfactory
18	63	F	24 hours' history of acute abdominal pain. Pulse 150, T. 101° F. (38·3° C.). On examination tenderness and rigidity of whole lower abdomen, more marked to right of midline	? Perforated appendiciticis. ? Perforated diverticulitis of colon	Gangrenous Meckel's diverticulitis with peritonitis	Simple excision of diverticulum, with satisfactory result

culum. It is more often seen in infancy and childhood, and is the only complication of Meckel's diverticulum other than umbilical lesions which can be diagnosed pre-operatively. The cardinal symptoms and signs are: (*a*) history of massive intestinal haemorrhage, (*b*) an average age of from 10 to 15 years, and (*c*) abdominal pain. Usually the patient gives a history of previous massive intestinal haemorrhage followed by a period of months, or even years, before recurrence. The haemorrhage is usually massive, although in some cases there may be a history of small and recurrent melaenas. Other conditions giving rise to rectal bleeding are Henoch's purpura, bleeding peptic ulcer, rectal polyp, ruptured rectal varicosities, and early congenital intestinal telangiectasis. In adults, benign and malignant tumours of the gastro-intestinal tract must also be considered. With careful examination it is usually possible to eliminate most of the conditions mentioned. The bleeding gastric or duodenal ulcer may, however, cause difficulty in the diagnosis, because some cases of diverticular ulcer do have a definite pain–food relation (see Case 15). Regardless of other symptoms, a history of massive haemorrhage from the rectum followed by recovery and then recurrence of haemorrhage after the lapse of weeks or months is almost pathognomonic of peptic ulcer of Meckel's diverticulum.

3. *Intestinal Obstruction.*—Meckel's diverticulum may be the cause of intestinal obstruction. The fibrous band connecting the diverticulum to the parietes or other adjacent organs may act as an axis about which the bowel may rotate to form a volvulus. At other times the diverticulum itself may be the leading point of an intussusception, particularly in the broad-based diverticulum. There is no characteristic feature to distinguish it from small-bowel obstruction due to other causes, but this condition must be borne in mind when confronted with a case of intestinal obstruction in infants and children.

4. *Umbilical Fistula and Associated Lesions.*—Lesions of the umbilicus associated with incomplete obliteration of the omphalo-mesenteric duct also occur, and are relatively easy to diagnose.

5. *Neoplasms.*—Tumours, both benign and malignant, have also been reported in Meckel's diverticulum, but are of rare occurrence.

6. *Foreign Bodies.*—Calculi and various foreign bodies have been encountered, giving rise in some instances to inflammation, perforation, and obstruction (see Case 18).

Treatment

It is generally agreed that silent diverticula found incidentally at laparotomy require no special treatment. It is only when a complication supervenes that the surgical treatment becomes a matter of urgency. The detail of operative procedure used must of necessity vary with the findings in the individual case. When intestinal obstruction is found, it is usually due to either a band or an intussusception. The band must be divided and the intussusception should be reduced, and, provided the general condition of the patient is satisfactory and there is no gross distension of bowel, the diverticulum may be resected at the same time. The method of excision, however, varies with different surgeons; some advise excision with closure of the defect by two rows of sutures, or by the same technique as used for appendicectomy, while others believe in resecting the diverticulum plus a portion of adjacent bowel, with subsequent anastomosis. With the former method particular care must be taken to avoid undue narrowing of the lumen. Ladd and Gross (1941) recommend that clamps should be placed at an angle of 45 degrees to the long axis of the bowel to reduce the risk of this complication. In cases of perforation or haemorrhage from an ulcer there is the possibility of heterotopic gastric mucosa extending up to the adjacent portion of the bowel, and it is therefore important to include it in the resection.

Cases of umbilical fistula or adenoma require formal laparotomy, as these conditions are commonly associated with incomplete obliteration of the omphalo-mesenteric duct, which should be remedied at the same time. In cases of diverticulitis with or without perforation, the general and local condition must be taken into account in deciding the advisability of resection of adjacent portions of the intestine. Diverticula which are sites of tumour formation should be excised, with a few inches of small intestine on each side, including a wedge of the mesentery.

The patients whose cases are reported in the Table were operated upon at Central Middlesex Hospital between 1936 and 1953. They illustrate well some of the more important complications of Meckel's diverticulum.

In seven of the cases the possibility of Meckel's diverticulum as the causative factor was considered, but in only three was the diagnosis made with some degree of confidence. The greater incidence of the condition in males in this series agrees with the findings generally recorded by other writers. There was one death in this series, giving a mortality of 5.5%. This occurred in a patient who was too ill for operation. Heterotopic gastric mucosa was found in two cases; some of the specimens were not submitted to histology, while in others there was no evidence of heterotopic tissue. However, without making several sections from each specimen, such tissue might readily be missed.

The complications of Meckel's diverticulum in childhood have been stressed by many writers, and, while such studies are entirely appropriate, the importance of these complications in adults must also be remembered. This is well shown in the Table, in which two-thirds of the cases were found in adults over the age of 21. In fact, in any acute abdominal emergency, unexplained bleeding from the gastro-intestinal tract, and vague intra-abdominal complaints the possibility of Meckel's diverticulum as the cause must be considered.

Summary and Conclusions

An account is given of the common complications of Meckel's diverticulum, together with a short note on treatment.

Eighteen cases, with one death, are reported and subjected to analysis.

The importance of Meckel's diverticulum as a cause of acute abdominal emergency, unexplained intestinal haemorrhage, or vague abdominal symptoms is stressed.

We wish to thank all members of the medical and surgical staff of the Central Middlesex Hospital, in particular Mr. T. G. I. James and Dr. F. Avery Jones, for their permission to publish these cases.

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The annual report of Yale Medical Library for the year ending June 30, 1953, includes some interesting information on the relative use made of medical periodicals. The library receives 1,140 serial publications of all types, and a rearrangement in the reading-room made it necessary to reduce the number of journals housed there. An analysis was therefore made of the recorded use of these journals, and it was noticed that the "current use" of a journal appears to continue for about five years, with the second year after publication being the time of heaviest use. It is shown that the availability of such periodicals is greatly increased if binding is delayed for five years. As much use was made of the two most popular journals together as was made of the 158 least popular on the list combined. Forty journals accounted for nearly half of the total use made of periodicals.

EARLY RECURRENT ACUTE INTUSSUSCEPTION IN CHILDREN

BY

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Acute intussusception in children is not a common condition. Spence and Court (1950) traced every child with this condition in the City of Newcastle-upon-Tyne during a six-year period and found the incidence was 3.8 per 1,000 births, or one case per family practitioner during that time. Recurrence of acute intussusception in children can be expected even less often. Thorndike (1932) reported five cases but found only 75 others in the literature. Since then Killins and Clagett (1941) and Mastin (1942) have described one case each, but the number even with the four cases reported here remains small. The following cases show that a recurrence can occur in the immediate post-operative period, a fact which does not seem to have been emphasized before.

Case 1

A female child aged 7 months was admitted to Bridgend General Hospital on January 22, 1950. She was an only child, was breast-fed until weaning one month previously, and had been quite well until the previous evening, when she began to have attacks of severe abdominal pain which, the mother stated, made the child draw up her knees. There had been some vomiting of food shortly after its ingestion. The bowels had been regular, but no action had occurred since the previous day. There were no urinary symptoms. On examination the child was seen to be in good general condition, and well nourished, and showed no signs of dehydration. Examination of the abdomen was difficult, as the child had repeated attacks of colic. No tumour was felt on abdominal or rectal examination, but whilst the latter was being performed the child had a bowel action with streaks of bright blood and mucus. A presumptive diagnosis of intussusception was made and operation undertaken immediately.

First Operation.—Under general anaesthesia a lower right paramedian incision was made and an ileo-colic intussusception was found, the apex of which had reached the splenic flexure. This was easily reduced. Enlarged mesenteric glands were noted but no cause was found for the intussusception.

The post-operative course was uneventful until January 30, when the child became restless and was obviously in some pain. There was mild infection of the wound but no physical signs were elicited on abdominal examination. Rectal examination revealed a small quantity of foul-smelling soft faeces but no blood. There was some dehydration which warranted an intravenous transfusion of half-strength Hartmann's solution. Examination of the urine showed a moderate growth of coliform organisms. On the following day the abdomen was obviously distended and the bowel sounds were greatly increased and high pitched. A diagnosis of acute small-bowel obstruction was made and laparotomy undertaken.

Second Operation.—Under general anaesthesia a lower left paramedian incision was made and an ileo-ileal intussusception was found with distension of the proximal small intestine. The origin of this intussusception was proximal to the previous one, the distal bowel now appearing normal, and, except for the enlarged mesenteric glands previously noted, no other abnormality was found. There was some superficial wound infection following the second operation which delayed convalescence, but the child was discharged in a month and was still well three years later.

Case 2

A female child aged 7 months was admitted to Bridgend General Hospital on May 11, 1950, with a history of repeated attacks of abdominal pain and vomiting for two days. She had also been passing blood and mucus per rectum for two days. Previously she had been a healthy child who was breast-fed until the age of 5 months, and had since then been fed on a proprietary milk food. On examination her general condition was good, she was having repeated attacks of abdominal colic, and a tumour was palpable in the left iliac fossa. On rectal examination a mass could be felt at the tip of the finger; it was continuous with the abdominal mass; there was blood on the examining finger; and a diagnosis of acute intussusception was made.

First Operation.—Under general anaesthesia a right paramedian incision was made. Two intussusceptions were found; an ileo-colic one originating just proximal to the caecum, and a colo-colic one in the left iliac fossa. The latter was antiperistaltic in the descending colon. The caecum, the ascending colon, and descending colon each had a long mesentery. The intussceptions were reduced without difficulty.

The post-operative course was normal until May 15, when the child again had spasms of abdominal pain and vomited copiously. The abdomen was not distended, but the bowel sounds were high pitched and increased, and rectal examination revealed some blood and mucus. Recurrent acute intussusception was diagnosed and laparotomy undertaken immediately.

Second Operation.—A lower left paramedian incision was made and some free fluid found in the peritoneal cavity. An ileo-ileal intussusception 8 to 9 in. (20 to 22.5 cm.) in length was situated 2 ft. (60 cm.) from the ileo-caecal valve, the proximal small intestine being greatly dilated. The intussusception was reduced. No apparent cause for the recurrence was found. The bowel at the sites of the previous intussusceptions was normal. The convalescence was uneventful, the child being discharged in three weeks. There had been no further recurrence on follow-up (1953).

Case 3

A previously healthy male child aged 2½ years was admitted to St. James's Hospital, Balham, on January 21, 1951, with a history of recurrent attacks of abdominal colic and vomiting for the past 36 hours. The bowels had not been open for 24 hours and there were no urinary symptoms. On examination the child was pale and looked ill, but there was no gross dehydration. Some tenderness was present in the right iliac fossa but no tumour was palpable in the abdomen. On rectal examination there was some bloody discharge on the examining finger. A presumptive diagnosis of intussusception was made, and operation performed immediately.

First Operation—A lower right paramedian incision was made under general anaesthesia and an ileo-ileal intussusception was found about 5 ft. (150 cm.) from the ligament of Treitz; it was reduced. No other abnormality or cause of the intussusception was found.

On January 24 vomiting of most feeds occurred, but no abdominal physical signs were found. Vomiting persisted, and on January 26 some signs of dehydration were apparent and a radiograph of the abdomen showed dilated loops of bowel in the upper abdomen with fluid levels. Laparotomy was immediately undertaken.

Second Operation.—Under general anaesthesia the previous wound was reopened and about 18 in. (45 cm.) from the ileo-caecal valve an ileo-ileal intussusception was found and reduced. A second intussusception about 8 ft. (240 cm.)

from the ileo-caecal valve was also reduced. The cause of the intussusceptions could not be found, and the site of the previous intussusception was normal. The child made an uneventful recovery and was discharged home on February 12.

Case 4

A female child aged 6 months was admitted to Llandough Hospital on October 29, 1952, with a history of vomiting after each feed two weeks earlier; this had become less, and four days before admission the child had had attacks of screaming and drawing up of the legs. She had vomited green fluid and had been constipated for two days, but had passed clots of blood per rectum on the day of admission; only small amounts of urine had been passed. On examination the child showed signs of severe dehydration. A large mass 3 in. (7.5 cm.) in length was palpable in the left iliac fossa, the apex of an intussusception was palpable per rectum, and there was blood on the examining finger. A diagnosis of acute intussusception was made.

First Operation.—The abdomen was opened through a lower right paramedian incision and an ileo-colic intussusception was found, extending to the pelvic colon. It was easily reduced.

On November 2 a loose green stool was passed. On November 4 the child vomited green material, the stool was relaxed and contained mucus. The abdomen was distended and tympanitic; bowel sounds were present. A radiograph of the abdomen showed distension of the small intestine. Treatment by intravenous fluids and gastric suction was begun, but as the condition did not improve laparotomy was undertaken on November 6.

Second Operation.—An ileo-ileal intussusception was found, 10 in. (25 cm.) from the ileo-caecal valve. There was no obvious cause for the intussusception. Convalescence was uneventful, the child being discharged on November 17.

The child was again admitted to the Cardiff Royal Infirmary on February 1, 1953, with a history of sudden onset of screaming and the passage of bright red blood per rectum on one occasion, but no vomiting. On examination the general condition was found to be good, no abnormality was noted in the abdomen, and a hard faecal mass was palpated in the rectum. Plain radiography of the abdomen showed no abnormality. On the following day the bowels opened normally, the child was discharged, and was well on follow-up on March 16, 1953.

Discussion

Killins and Clagett (1941) reported a case of recurrent intussusception at the Mayo Clinic and believed the condition to be rare. They further stated that "the patient, by undergoing two successful operations for intussusception, has become something of a surgical curiosity." Thorndike (1932), in searching the records of the Children's Hospital, Boston, found that 405 cases of acute intussusception in children had been admitted between 1869 and 1932, and of these only five had had post-operative recurrences, which is a ratio of about one in 80. As intussusception itself is not overcommon, this means that a small but nevertheless important number may go on to recurrence. Mastin (1942) reported a case in which three separate intussusceptions took place within twelve months.

The period of time between the initial attack and the recurrence varies considerably. In Thorndike's series the average time was five months and in all his cases the patient had left hospital. Arntzen and Helsted (1929) reported the longest interval between the initial attack and recurrence of eight years, whilst Cohen (1921) reported a case occurring 30 hours after operation. The cases reported above recurred at eight, four, five, and six days respectively after operation, and come into some of the earliest groups recorded.

The cause of acute intussusception when there is no underlying disease such as a tumour or Meckel's diverticulum is still unsettled and theories involving neuromuscular dysfunction and enlarged Peyer's patches still remain unproved. It is therefore not surprising that there is no satisfactory theory for the recurrence of acute intussusception. Mastin (1942) stated that in more than half the cases of acute intussusception the caecum was found to be mobile, and that he anchored the latter in the right iliac fossa. This caecal mobility was present in Case 2, and the long mesentery in both ascending and descending colon may well have been an aetiological factor in the causation of the original intussusception, but it does not explain the recurrence, which was ileo-ileal in origin. In Cases 1, 3, and 4 there was no mobility of the caecum.

Conclusion

Recurrent acute intussusception in children, although rare, is a condition to be borne in mind even in the early post-operative days, and careful observation of these small patients is recommended so that laparotomy may be undertaken early in this condition. The diagnosis is easier to make when there is a longer interval and the patient has been discharged from hospital, but in the post-operative period it may easily be overlooked and an incorrect diagnosis made because the child has already had an intussusception. We wish to draw attention to this possibility of early post-operative recurrence so that treatment may be undertaken. Immediate operation is the form of treatment recommended, and, as imbalance very readily occurs, attention should be paid to the fluid requirements of the child, intravenous infusion being carried out if necessary. If there is a mobile caecum the anchoring of this is suggested as a measure that may prevent further recurrence, but if no such mobility exists no further treatment other than the reduction of the intussusception can be advised until the aetiology of the condition is more fully understood.

Summary

Four cases of early recurrent acute intussusception in children treated successfully are reported.

The rarity and importance of the condition are shown.

The importance of early diagnosis, based on the clinical state and radiological findings, is emphasized.

The treatment is operative, with reduction of the intussusception.

We would like to express our thanks to Dr. Jeffrey W. Jones for permission to publish Cases 1 and 2, to Mr. Norman C. Tanner for Case 3, and Professor A. G. Watkins and Mr. D. B. E. Foster for Case 4; to Mr. F. J. Hedden who performed the original operation in Case 1, to Mr. D. H. Teasdale in Case 3, and Mr. H. Millard in Case 4. Our thanks are also due to Mr. N. C. Tanner and Mr. A. M. Desmond for their helpful criticism of this paper.

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At Harrow trust funds of about £20,000 of the former district nursing association are to be used to establish a physiotherapy service for residents confined to their homes. Treatment will be restricted to the less well off, who will pay varying charges according to their means or receive it free if in needy circumstances. The diagnosis and prescription of the family doctor will be sufficient for the physiotherapist to proceed with treatment. It is expected that local private physiotherapists will be willing to undertake the service, but if that is not possible a van, or vans, equipped with apparatus and in charge of a driver-physiotherapist will be used.

CRANIOSTENOSIS WITH FAMILIAL VITAMIN-D-RESISTANT RICKETS

BY

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The syndrome of rickets resistant to normal therapeutic doses of vitamin D but amenable to treatment with massive doses (up to 1,500,000 i.u. daily) was first described by Albright, Butler, and Bloomberg (1937). Since then the literature has become extensive, and it is now recognized that the condition is by no means rare. Holt (1950), Scott (1951), and Pedersen and McCarroll (1951) give good accounts of it; the latter, in the course of an account of 25 cases, point out the strongly familial nature of the disease. Albright *et al.* established by metabolic studies that there is a resistance to normal doses of vitamin D not attributable to malabsorption of the vitamin; and Robertson, Harris, and McCune (1942) attribute the complaint to deficiency of an enzyme, of which vitamin D is said to be the prosthetic group, normally responsible for absorption of phosphate by the gut and its retention by the kidney. Freeman and Dunsky (1950), however, failed to get a restoration of normal serum phosphate despite successful therapy, and they question whether vitamin-D treatment corrects the metabolic defect.

FIG. 1.—The patient aged 6¼ (right), with his brother aged 5¼.

FIG. 2.—Active rickets (aged 3).

FIG. 3.—Improvement (aged 6¼).

The deformities occurring in vitamin-D-resistant rickets are similar to those of classical rickets; indeed, there is no reason to suppose that the mechanism of deformity is in any way different in the two conditions. In one respect, however, there appears to be a difference—that in the familial resistant variety craniostenosis occasionally occurs. This has been stated only once in the literature, by Imerslund (1951), who describes a boy with typical vitamin-D-resistant rickets whose mother has old rachitic deformities. This child has a considerable degree of scaphocephaly following on premature fusion of the sagittal suture, and necessitating craniotomy for the relief of increased intracranial pressure.

This is not the only occasion on which scaphocephaly has been reported, for it is evident in an illustration of one of the cases of Albright *et al.*, and Pedersen and McCarroll mention the deformity while attributing it to rickets. In addition, Scott comments on the existence, in some cases, of frontal bossing with increased antero-posterior skull diameter and decreased transverse measurement. None of these authors, however, make mention of craniostenosis due to premature fusion of the sagittal suture, which clearly occurred in Imerslund's patient, whose mother also showed a small degree of scaphocephaly. No attempt has been made to explain this association of conditions, the one manifested as delay in ossification, the other by its premature occurrence. We regard this association as unusual enough to warrant the following description of a second case showing both phenomena.

Case Report

A boy aged 6 was first diagnosed as suffering from classical rickets when 2–3 years old. He is the eldest of three, the third child having died of meningitis in infancy. Fig. 1 shows the patient with his younger brother. All three were born by caesarean section, as the mother has old rickets with a contracted pelvis and genu valgum. She has no obvious biochemical abnormality apart from the rather low figure of 1.7 mg. of phosphorus per 100 ml. for her plasma inorganic phosphate. She has not got scaphocephaly. No relevant family history was obtained, as the family is not particularly "clannish" and little is known of some relatives. The patient had a normal diet as an infant and an adequate supplement of national cod-liver oil—2 dr. (7 ml.) daily from 1 year onwards. Despite this he developed frank rickets when 2 years old. A photograph (too "grainy" for repro-

duction) at 20 months shows him walking normally, but with the skull deformity already apparent. At 3 years he had active rickets (Fig. 2). He was given routine anti-rachitic treatment (sunlight and fish-liver oils). When first seen by us in August, 1952, at 6¼ years, his wrists were as shown in Fig. 3. His skull deformity is shown in Figs. 4 and 5.

Biochemical Investigations (in each case the mean of two or more estimates is given).—Serum calcium, 10.2 mg. per 100 ml.; plasma inorganic phosphate, 2 mg. of phosphorus per 100 ml.; alkaline phosphatase, 31 King–Armstrong units; blood urea, 26 mg. per 100 ml.; urea-clearance test (Van Slyke), 120% of average normal; urine, N.A.D. on numerous occasions. In addition the following were found on one occasion each: plasma chloride, 100 mEq per litre; alkali reserve, 27 mEq per litre; fasting blood sugar, 88 mg. per 100 ml.; faecal fat, 15.7 g. per 100 g. dried faeces (unsplit, 1.4 g.); three-day fat balance, absorption 94%.

After treatment with 50,000 i.u. of vitamin D daily by mouth, starting in early September, 1952, the serum calcium rose slightly to 11.2 mg. and the plasma inorganic phosphate rose progressively to 2.7 mg. after three weeks and to 4.3 mg. in six weeks, but fell to 2.4 mg. after 25 weeks of the same treatment. The alkaline phosphatase did not vary significantly over this period. The only definite biochemical abnormalities were the low plasma inorganic phosphate and the slightly raised phosphatase. The former responded temporarily to the relatively small dose of vitamin D. Renal function remained normal throughout.

FIG. 4.—The patient aged 6¼.

We are indebted to Dr. C. H. Wood, for the following report: "November, 1948:—Generalized decalcification with bowing of long bones; widening of the space between epiphyses and metaphyses; saucer-shaped and irregular metaphyses; these changes are more advanced in the legs. Skull: marked scaphocephaly with closure of the sagittal suture. August, 1952:—Appreciable improvement since earlier films, although not healed. February, 1953:—Improvement maintained, but still not healed; *x*-ray films of patient's mother showed typical changes of healed rickets but no scaphocephaly."

FIG. 5.—Skull (aged 6¼).

There seemed to be little doubt of the diagnosis of vitamin-D-resistant rickets, and more vigorous therapy was instituted. In addition he has well-marked craniostenosis from premature fusion of his sagittal suture, a condition only once previously described in association with resistant rickets.

Summary

The second reported case of craniostenosis associated with vitamin-D-resistant rickets is presented together with evidence to suggest that the association of these conditions may have occurred previously and been mistaken for a purely rachitic phenomenon.

We are indebted to Dr. J. M. Macfie for permission to publish this case; to Dr. C. H. Wood for the *x*-ray films; and to the department of clinical photography, General Hospital, Nottingham, for the other illustrations.

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ANAESTHESIA IN HOSPITAL BREECH DELIVERY

BY

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For practical purposes an infant may be delivered by the breech in one of two very different ways: an assisted breech delivery or breech extraction. The two essential features of the former type of delivery are that labour should be left to the natural forces so far as possible and that any intervention should imitate the normal mechanism of breech delivery. In practice this implies that assistance is confined to the birth of the arms and, more especially, of the head. In contradistinction to an assisted breech delivery, delivery in a breech extraction is entirely operative, the maternal powers playing no part. In most cases intervention is undertaken before the breech has started to distend the vulva, the legs being brought down and delivery completed by a combination of traction and gentle fundal pressure.

In the absence of definite indications for early delivery, choice of methods is dictated by consideration of the foetal hazards. These have been shown to be due to two factors—namely, trauma and anoxia, of which the former is by far the more

common. Although trauma may at times be due to disproportion, in the great majority of instances it may be directly ascribed to one or more of the following causes: undue manipulation of the foetus; manipulation carried out under difficulties; and uncontrolled delivery of the after-coming head. Ideally, therefore, an assisted breech delivery should always be aimed at, since it demands the minimum of intervention. Where, however, indications arise for a breech extraction, it is important that the necessary manipulations—which often involve the passing of the whole hand into the uterine cavity—should be rendered as atraumatic as possible by ensuring good relaxation not only of the perineal floor but also of the uterus itself.

In addition, in both these methods of delivery the foetus may have to undergo a period of oxygen deprivation before delivery of the mouth.

From what has been said, it will be evident that the anaesthetic requirements in breech delivery will to a large extent depend upon the obstetric procedure decided on. Thus, in an assisted breech delivery there must be good oxygenation, restraint in inducing anaesthesia prematurely at a time when reliance should be placed upon the mother's expulsive powers, and rapid and smooth induction of anaesthesia when this is finally necessary. In a breech extraction, on the other hand, as well as good oxygenation there must be good relaxation both of the uterus and of the muscles of the perineal floor.

Analgesia.—No contraindication exists to pethidine, given in doses of 100–150 mg. (Nixon and Ransom, 1951) during the first stage of a breech delivery. Although that drug may depress the foetal respiratory centre to a slight extent, this is not necessarily a disadvantage, since respiratory efforts are best delayed until after the delivery of the mouth. Inhalation analgesia may be required at times to supplement the effect of pethidine. For the period preceding the birth of the breech a nitrous oxide and oxygen mixture (75% and 25%) has the advantage of providing good oxygenation.

Assisted Breech Delivery

Perineotomy

This operation is an essential procedure in all primiparae and in most multiparae. It should be deferred until the breech is widely distending the perineum, in order to reduce the amount of blood loss. The incision should be made under local infiltration analgesia, preferably 1% lignocaine hydrochloride ("xylocaine"). By this means, despite a temporary inhibition of the perineal reflex, strong expulsive efforts usually return within two to three minutes and result in the spontaneous delivery of the breech and trunk.

Some workers (Urnes and Timerman, 1937; Greig, 1945; Trites, 1948) prefer pudendal block to the local infiltration described above, it being claimed that this procedure gives enough analgesia for the safe and painless completion of delivery. In experienced hands this is a valuable method for selected cases, but it possesses certain disadvantages: (1) If it is carried out too soon the resulting interference with the perineal reflex reduces the incidence of spontaneous delivery of the breech, and early intervention is correspondingly more common. (2) If, in order to derive the maximum benefit from the mother's expulsive efforts, analgesia is delayed until the breech is distending the perineum, it may be impossible to reach the ischial spines. The pudendal nerve must then be blocked at its exit from Alcock's canal at the ischial tuberosities. Since this point cannot at times be determined with accuracy, the resultant analgesia may be insufficient for the routine application of forceps to the after-coming head, a procedure which we strongly advocate in all cases. (3) The extent of analgesia is insufficient for the safe and effective correction of some of the complications which may arise in the course of delivery.

Delivery of the Arms and Head

While in agreement with a policy of minimal intervention in assisted breech deliveries, we do, however, feel that if carried to excess it imposes a definite risk on the foetus. Occasions may arise, especially in relation to the delivery of the after-coming head, when, owing to unforeseen difficulties, simple measures do not suffice and a sudden need for anaesthesia arises often after loss of much valuable time. It is therefore our custom to allow spontaneous delivery to proceed only until the angles of the scapulae are visible. At this stage anaesthesia is induced, after which the arms are brought down by Løvset's manœuvre and the forceps applied to the after-coming head.

As already stated, the chief anaesthetic requirements in this type of delivery are that induction should be smooth and swift while maintaining good oxygenation. Every experienced anaesthetist develops his own techniques with which he produces the best results, but for the benefit of those approaching this problem for the first time we feel that mention should be made of some disadvantages of two common methods of induction: (1) thiopentone, and (2) gas, oxygen, and ether. Thiopentone sodium (5% solution) has many advocates (Dippel *et al.*, 1947; Kerr and Moir, 1949; Cox, 1950; Calverley, 1950; Dewhurst, 1952), and at first sight would seem to fulfil all requirements. It is, however, widely felt that the danger of regurgitation and inhalation of stomach contents is a contraindication to the extended use of this substance. With gas, oxygen, and ether, induction is either too slow for the purpose under discussion, or, should induction be deliberately hastened, a period of reduced oxygen intake often results.

We would like to suggest that divinyl ether has properties which recommend it for use in assisted breech deliveries. It may be given in a variety of ways, our preference being to combine it in a closed circuit with oxygen and cyclopropane. After this, anaesthesia may be continued with any suitable mixture, such as gas, oxygen, and ether.

Some obstetricians (Allan, 1935; Rosenfeld, 1940; Cunningham, 1945) recommend that general anaesthesia be induced as soon as the perineum is distended by the breech. We do not, however, subscribe to this view, since the resultant interference with voluntary expulsive efforts substantially increases the frequency and extent of operative intervention. For the same reason low spinal or extradural anaesthesia (Urnes and Timerman, 1937; Kerr and Moir, 1949) are unsatisfactory. In addition, in the case of spinal anaesthesia there is a slight but definite risk associated with the injection of foreign material into the cerebrospinal fluid.

Neither of the two methods referred to above outweighs in advantages a general anaesthetic withheld until the correct moment—a procedure which is easy to perfect, given the proper degree of co-operation between anaesthetist and obstetrician.

Breech Extraction

In this type of breech delivery the need for a rapid induction is no longer present, while good relaxation of the uterus and of the muscles of the perineal floor is essential if trauma is to be avoided (Potter, 1922; Piper and Bachman, 1929; Greig, 1945; Gustafson, 1949). This in effect means that a sufficiently deep ether anaesthesia must be given, since the use of the only other uterine relaxant—namely, chloroform—is unjustifiable in hospital practice. It might be thought that the degree of foetal narcosis thus produced would be hazardous, but in any event this is preferable to trauma, and in practice seldom gives rise to anxiety.

Drugs such as thiopentone, cyclopropane, and curare are on the whole unsuited to the procedure under consideration, since, although they may or may not produce a rise of uterine tone, they certainly do not relax the uterus.

On the other hand, a spinal or extradural anaesthetic given to a height sufficient to abolish uterine sensation does cause a considerably "heightened reactivity" to stimuli of the uterus (Malpas, 1944; Lull and Hingson, 1948). As a result not only is the risk of trauma both to the foetus and to the mother greatly increased, but, in addition, foetal anoxia may arise owing to placental ischaemia. This form of anaesthesia is therefore entirely contraindicated in breech extraction.

Considerations with Regard to the Third Stage.—A possible argument against the use of ether in breech extraction is that the resultant lowering of uterine tone might predispose to serious post-partum haemorrhage. It is probable, however, that this complication has been over-emphasized in the past; certainly in our experience it has rarely been observed. This may be due to the fact that it has always been our policy to give 0.5 mg. of ergometrine intravenously following the birth of the head. At all events, the danger of a contracted uterus during breech extraction would seem considerably to outweigh that of a relaxed uterus after delivery has been completed.

Summary

Assisted breech delivery and breech extraction are two very distinct obstetric operations requiring different anaesthetic techniques.

The special considerations involved in anaesthesia for such deliveries have been reviewed.

In assisted breech delivery it is recommended that a perineotomy be performed under local infiltration analgesia, inhalation anaesthesia being limited to the delivery of the arms and head.

In breech extraction a high degree of uterine relaxation is necessary. For this reason a deep ether anaesthetic is the only one which may justifiably be employed.

Spinal or extradural anaesthetics are not the most suitable for assisted breech deliveries and are absolutely contraindicated in breech extraction.

Close co-operation between obstetrician and anaesthetist is essential if the best results are to be obtained in this branch of obstetrics.

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Conservancy Systems at Collieries is the title of a medical memorandum recently issued by the National Coal Board. It is intended as a general guide for colliery managers. After stating the legal requirements, the memorandum describes various installations for use above or below ground. The standard of sanitation in mines is, not surprisingly, below that in other industries. Both health and morale would benefit if it were improved.

DANGERS OF POLYPHARMACEUTICAL PREPARATIONS CONTAINING FOLIC ACID

BY

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The inclusion of folic acid in proprietary preparations was deplored by Davidson (1948), but, as can be seen from the examination of recent advertising matter, the practice continues. The purpose of this note is to draw attention to the difficulties which may arise when anti-anaemia treatment is undertaken without proper investigation of the case and with preparations of the "blunderbuss" type.

Case Report

A 46-year-old housewife first complained of stiffness of her knees in October, 1952. Treatment with short-wave diathermy was given after she had attended orthopaedic and medical dispensaries. In January, 1953, she developed a short febrile illness associated with vomiting, anorexia, and loss of weight, from which she did not fully recover. In February, at another medical dispensary, no abnormality was found on examination, with the exception of a haemoglobin level of 48% (Sahli). A course of iron was recommended, and the patient was requested to attend for further investigations. Her family doctor gave her a proprietary preparation of iron, and her general condition improved greatly. Her appetite returned to normal and her weight increased, but the stiffness of her legs began to worsen rapidly. She did not return for investigation, but in May, 1953, she fell and was admitted to hospital for treatment of an infected haematoma. After 10 days in bed she was found to be unable to rise or walk, and was transferred to a medical ward for investigation.

On examination the patient was found to have a spastic paraplegia with great muscular weakness, bilateral extensor plantar responses, and complete loss of posterior column sensation in both legs. There was no upset of the function of bladder or bowels. Histamine-fast achlorhydria was demonstrated. Blood examination showed: haemoglobin, 12.3 g.%; red cells, 3,600,000 per c.mm.; white cells, 8,000 per c.mm.; P.C.V., 38%; M.C.V., 105.6 μ^3; M.C.H.C., 32.1%. Sternal marrow biopsy showed appearances suggesting a partially treated anaemia resulting from deficiency of the haemopoietic principle. Lumbar puncture and radioscopy of the lumbar spine showed no abnormality.

A diagnosis of subacute combined degeneration of the cord was made, and treatment with "anahaemin" and vitamin B_{12} was started (4 ml. of anahaemin on alternate days, and 100 μg. of "cytamen" daily). Haematological and neurological improvement was rapid, and five weeks later the patient was walking well enough to continue treatment as an out-patient. When last seen she had only very slight ataxia, and examination of the blood and marrow showed normal appearances.

It was found that she had been treated originally with capsules containing iron, vitamin B, extract of raw liver, and folic acid. The amount of folic acid present in each capsule was 1 mg., and she had consumed 3 mg. of folic acid daily for 38 days.

Discussion

The literature on the results of treatment of cases of Addisonian anaemia with folic acid was reviewed by Davidson (1948) and by Israëls and Wilkinson (1949). These authors concluded that folic acid had no place in the treatment of pernicious anaemia. The haematological state not

infrequently remains unsatisfactory (Wilkinson, 1948), and the neurological state is not prevented from deteriorating (Davidson, 1948; Israëls and Wilkinson, 1949). Since then Fuld (1950) and Schwartz *et al.* (1950) have reported poor haematological and neurological results with folic acid therapy. The latter reported 72 cases followed for three and a half years and treated with 5 mg. of folic acid daily: 23 cases developed cord degeneration, in 23 the red cell count and marrow showed relapse, and in 9 cases both occurred. Subacute combined degeneration of the cord has been reported as occurring with doses varying between 5 and 25 mg. daily. In the present case 3 mg. daily was enough to produce a considerable improvement in the blood condition, but did not prevent the rapid development of paraplegia.

In at least two large series folic acid has been given to normal subjects and to cases of anaemia other than pernicious anaemia (Weissberg *et al.*, 1950; Harvey *et al.*, 1950). There was no subsequent development of cord degeneration, and it is thus unlikely that folic acid has any direct toxic effect. The following reports of authors who have had the opportunity of observing large numbers of cases of Addisonian anaemia contain statements which suggest that they have not rejected the possibility that folic acid actually precipitates cord disease. Thus the explosive character of the onset of cord disease, as well as its rapid progression, have been more often noted after folic acid therapy, and have been contrasted with the more insidious disease previously described (Davidson, 1948; Wilkinson, 1948; Ross *et al.*, 1948; Jacobson *et al.*, 1948). The present case also showed these more acute features.

The experience of Conley and Krevans (1951) is interesting, being more akin to the present case. These authors saw 10 patients in 1950 who were suffering from undiagnosed Addisonian anaemia. Five had only neurological symptoms with no associated anaemia, and on this account various diagnoses, such as disseminated sclerosis and syphilis, were entertained. It was established that four out of the five had been given multivitamin preparations containing folic acid. The patients were not aware that they had received anti-anaemic treatment, and in two cases the physician prescribing the capsules was unaware that they contained folic acid. In all cases an excellent response to vitamin B_{12} was obtained. It was therefore suggested that in all doubtful cases a marked improvement in nervous system signs and symptoms following the injection of vitamin B_{12} provides strong support for a diagnosis of Addisonian anaemia.

The arguments against the inclusion of folic acid in polypharmaceutical preparations may be summed up as follows: (1) Folic acid temporarily improves the blood picture, and may restore it to normal. The physician is then faced with a disease of the central nervous system, the misdiagnosis of which is likely, as subacute combined degeneration of the cord without anaemia is very uncommon. (2) The relief of the general symptoms of pernicious anaemia often reassures the patient and the doctor, and masks the deterioration of the nervous system. (3) Folic acid deficiency occurs infrequently, and there is no need for this substance in multivitamin or iron preparations. (4) The question whether folic acid actually precipitates cord degeneration is still uncertain.

Summary

A case is described in which a proprietary preparation of iron containing folic acid was given to a patient with an anaemia which had not been accurately diagnosed. In fact, the patient was suffering from Addisonian anaemia. Deceptive improvement in the blood condition occurred, but was accompanied by the rapid development of combined degeneration of the cord.

My thanks are due to Dr. J. A. W. McCluskie, in whose ward the patient was treated; to Dr. S. Lazarus for encouragement and helpful suggestions; and to Miss N. Johnston for secretarial aid.

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Medical Memoranda

Carbon Dioxide Retention Simulating Curarization

Numerous reports have appeared of persistent curarization after the use of one or other of the relaxants; the following case therefore seems worthy of description.

CASE REPORT

The patient, a child aged 6, weighing 42 lb. (19 kg.), had undergone a laparotomy for the removal of a polyp from the sigmoid colon.

The premedication consisted of pentobarbitone sodium, 2 gr. (0.13 g.), and atropine, 1/100 gr. (0.65 mg.), following which the child arrived at the theatre asleep. Anaesthesia was maintained with nitrous oxide and oxygen and a trace of ether, a size 3 endotracheal tube having been inserted. The flow was at the rate of 3 litres of nitrous oxide and 2 litres of oxygen a minute. No absorber was incorporated. Just before opening the peritoneum 2 mg. of decamethonium iodide was given intravenously. After a brief period of apnoea respiration returned and was accompanied by a satisfactory degree of relaxation. (The respiration was assisted throughout.) Some 15 minutes after the first dose a second injection of 2 mg. of decamethonium iodide was given. This time the apnoea persisted for 15 minutes, and at the time of the skin closure only minimal diaphragmatic respiration was present.

After an interval of five minutes, respiratory activity, although minimal, appeared just sufficient to keep the child a good colour, provided pure oxygen was given through a T-piece connected to the endotracheal tube. The child was therefore returned to bed with a flow of 5 litres of oxygen a minute passing through the T-piece, and inflation by means of a bag was carried out for one-minute periods every five minutes.

Respiratory activity did not increase, although the child at all times remained a very good colour, there being no evidence of suboxygenation. After two hours it was noted that, if anything, respiratory activity was decreasing again, but that there was some improvement after each period of ventilation. There was no response at all to an intravenous dose of 2 ml. of nikethamide. The delay in recovery of respiration had until this time been attributed to a residual effect of the decamethonium iodide; but it was noted that such respiratory effort as was present was not marked by any urgency, neither was it accompanied by a tracheal tug, both of which features are usually present in cases of residual curarization.

Three hours after the injection of the second dose of decamethonium iodide, on the supposition that carbon dioxide accumulation might be the underlying cause of the respiratory depression, the child was vigorously hyperventilated through an absorber for a period of three minutes. The absorber very rapidly became intensely hot, indicating considerable elimination of carbon dioxide. Promptly following this hyperventilation the child's respiration was noted

to be greatly increased in depth, and therefore a further three-minute period of hyperventilation through the canister was undertaken. At the end of this the child's respiration was noted to be normal in depth and character. The endotracheal tube was therefore removed, and an airway was substituted. No further oxygen administration was required.

COMMENT

The remarkable features of this case appear to be: (1) Persistent respiratory paralysis, apparently due to the residual effect of a relaxant, seems to have been caused by carbon dioxide retention. Possibly an increased carbon dioxide tension is capable of producing myoneural block. (2) The child did not recover consciousness for some four hours, although recovery would normally have been anticipated within one hour after operation; it therefore seems likely that the degree of carbon dioxide retention was sufficient to produce narcosis.

It is unfortunate that carbon dioxide estimations were not possible in this case. The difficulty of the treatment of prolonged respiratory depression is illustrated. Such depression has been attributed to hyperventilation: it now appears that underventilation also may perpetuate respiratory depression. It is possible that an electronic apparatus may in future be devised which, by means of an electrode inserted into the tissues, may give continuous measurement either of *p*H or of carbon dioxide concentration. Such an instrument would obviously be of the greatest value in cases requiring controlled ventilation.

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A Possible Method of Pre-operative Anticipation of Thrombo-Embolic Episodes

In recent years major advances have been made in the preparation of patients for the stress and eventualities of surgical procedures, and many previously fatal secondary factors can now be evaluated and corrected pre-operatively to prevent a fatal outcome. Not so post-operative thrombo-embolic episodes: the majority still occur apparently unexpectedly and in spite of increasing awareness of the condition and diligent attempts to anticipate its occurrence.

Ochsner has shown that approximately 50% of pulmonary emboli occur in patients without recognizable preceding peripheral stigmata. Sulamaa and Pentti (1949) reported 170 cases of thrombo-embolic disease, 20 being fatal pulmonary emboli: of the latter, 14 were not diagnosed or were not suspected before their occurrence. Felder (1949) reported 27 cases of pulmonary emboli; in 10 the chest and peripheral signs occurred simultaneously and in 11 cases the chest signs were the first indication. In 78% of his cases treatment began after the chest signs were manifest.

Active prophylactic therapy, excluding routine use of anticoagulants, has not lowered the incidence; 0.57% of patients are liable to pulmonary infarction and 0.22% to fatal pulmonary emboli. A perusal of gastrectomy fatalities shows that about 20% are due to pulmonary emboli.

It is thus the more apparent that pre-operative diagnosis of the thrombophilic type of patient would present a major advance in the selection of those patients who require post-operative anticoagulant therapy. At present it would be unwise to adopt routine anticoagulant treatment owing to its cost, its sequelae, and the labour involved.

It seems reasonable to postulate that clotting *per se* is a normal physiological accompaniment to wound-healing, and that in association with any trauma, definitive or accidental, there is a general and a local mechanism which ensures clotting at the breaches in vascular continuity; likewise, this process is graded in degree to meet the local requirement, and its duration should be proportional to the initial lesion. This effector mechanism has already been discussed in detail by many authors, and no useful purpose will be served by repeating their observations.

Previous attempts have been made to prevent patients from developing thrombo-embolic episodes—the construction of a coagulation graph post-operatively and detection of fibrinogen B in the plasma (Cummine and Lyons, 1948). Ochsner also propounded the theory of a lowered antithrombin titre, and advocated the use of alpha-tocopherol and intravenous injections of calcium to raise a lowered titre. No case selection was made, and such a method, even if it proved to be effective, would be costly and, like coagulation-graph charting, could be conducted only in well-staffed institutions. If it could be foreseen which patients were liable to thrombo-embolic phenomena, active measures could be taken with this smaller group.

It is possible that an increased post-operative clotting tendency is a function of the general response of the body to the strain applied to it by a surgical operation and that the degree of clotting is an indication of adrenal cortical function. During recent years there have been increasing records of spontaneous thromboses and embolic phenomena occurring during cortisone therapy. Cosgriff (1951) recorded the increased coagulability of the blood during treatment and an unexpectedly high incidence of thrombo-embolic complications. The patient liable to post-operative thrombotic episodes may thus respond abnormally to stress or prolongation of the post-operative state.

Godlowski (1951) demonstrated that changes in the eosinophil count could be modified by the administration of heparin, and this suggested that such changes may bear some relation to blood coagulability. Post-operative eosinophil counts were charted on several cases, but the results were not uniform.

An effective reproduction of stress to the body can be secured by the adrenaline test, as used extensively in America to ascertain the resistance to stress of a patient about to undergo a given major operation.

Adrenaline hydrochloride, 0.3 mg., was given to pre-operative patients, and their clotting-times and eosinophil counts were recorded half-hourly during the next four hours. It was found that varying results were obtained. These same patients had coagulation graphs taken post-operatively and were examined clinically for thrombotic stigmata. In all, about 50 patients have been examined and a certain pattern is developing.

The majority of those patients examined showed a rapid shortening of their coagulation time during the first hour and then a fairly quick return to normal time inside the four-hour period of examination. Six of them showed a shortened coagulation time, but it persisted at a low level and was still present after six hours. They also were followed up post-operatively, and all six developed thrombotic episodes, two of a major nature and one fatal. The other patients demonstrated shortening of their coagulation time for four days and then elongation to normal.

All patients were treated identically: pre-operative and post-operative physiotherapy, early rising, and routine examination for tender calf muscles and calf-muscle spasms. The duration of stay on the operating table was almost identical, and the operative procedures were of a similar magnitude and location.

Application.—Given forewarning of subjects who are likely to develop post-operative thrombotic episodes, it is possible to provide selective treatment with anticoagulants 24–48 hours after operation; and, in the event of the discovery of a more innocuous replacement therapy on the lines of the antithrombin hypothesis, treatment could be given post-operatively to those subjects showing a suggestive adrenaline response and liable to undergo major surgery.

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Reviews

DISEASES OF MUSCLE

Diseases of Muscle: A Study in Pathology. By Raymond D. Adams, M.A., M.D., D. Denny-Brown, M.D., D.Phil., F.R.C.P., and Carl M. Pearson, M.D. (Pp. 556; 347 illustrations. £5 18s. 6d.) London: Cassell and Company. 1953.

It is quite surprising that before this monograph was written there was no comprehensive and critical account of the diseases of skeletal muscle in the medical, surgical, or neurological literature of this country or America. The deficiency becomes all the more remarkable when, after even a brief perusal of this almost encyclopaedic volume, one appreciates how fascinating the study of skeletal muscle can be made when its development, structure, and function are skilfully related to its behaviour in the wide variety of diseases and injuries in which it participates.

The monograph is divided into two parts. The first is on the nature of skeletal muscle, including its embryology, anatomy, and histology, the chemistry and physiology of muscular contraction, and its general pathology. This last section must be unique in pathological literature. It deals with the large volume of widely scattered observations relating to the experimental pathology of muscle and is followed by a description of the basic pathology of human muscle.

This first part on anatomy, physiology, and general pathology serves as an introduction to the second. This covers the special pathology of myopathic diseases, and, though it is primarily concerned with pathology, informative and concise surveys of the clinical background clearly define the disease entities. There are several useful chapters in this well-illustrated section, which includes the pathology of the muscular dystrophies, myositis in general, the effects of ischaemia, spinal and neuronal atrophy, and toxic metabolic and endocrine disorders, and a remarkably informative chapter on disorders of excitability and contraction. The account of myasthenia gravis is outstanding.

Taken as a whole, the book contains a large number of reviews of subjects which have not yet reached the orthodox textbooks. Among these reviews are accounts of haemopoiesis in skeletal muscle, fibril structures of muscle by electron microscopy, the part played by venous occlusion in obliterative vascular disease, the remarkable resistance of muscle to several poisons and to irradiation, and its equally remarkable susceptibility to certain quinoline compounds, to Coxsackie virus, vitamin-E deficiency, and variations in the potassium content of the plasma.

Workers in many fields will be indebted to the authors for the thoroughness with which they have collected and skilfully analysed an enormous amount of relevant information. There are many references; the illustrations are of the highest standard, and a large proportion will be new to most general readers. The substantial contributions to the subject made by the authors themselves stamp their monograph with authority. This is certainly a book which every serious student of disease must acquire.

GEOFFREY HADFIELD.

INDUSTRIAL PHYSIOLOGY

Praktische Arbeitsphysiologie. By Professor Gunther Lehmann. (Pp. 352; 145 figures. M.33.) Stuttgart: Georg Thieme. 1953.

Analysis of human endeavour, and study of the conditions of human endurance and comfort, in peace and in war, at work or at sport, has often engaged the attention of physiologists. It is especially in the highly industrialized countries that the scientific study of the conditions of human labour is of high importance, for, in the author's opening words, "Working man is the most important and valuable factor in production." This book, by the distinguished director of a world-famous institute for the study of working conditions, is written not only for physiologists but for all who have the responsibility for the scientific organization and amelioration of the conditions under which all sorts of work is done. It is of importance, therefore, for those with managerial responsibilities. Physiological theory as commonly understood has little place in it, for the outlook is rather that of an *ad hoc* approach to the many problems which affect conditions of effort, gainful or otherwise.

Problems discussed include those of the purely mechanical type, such as static and dynamic effort, co-ordination, fatigue, rest, accommodation, age and sex, climate, energetics, and the adaptation of machines to the individual. Most of the illustrative material is derived from studies in which the author or his colleagues have been engaged. As the recent inauguration and subsequent rapid growth of the Ergonomics Research Society in this country shows, these subjects now engage the attention of numerous experts, and there is already good progress to report. This book will set them a high standard to live up to, and will do much to disseminate useful information. Author and publishers are to be congratulated on having done a service in the interest of good industrial relations, as well as in the interests of science.

C. LOVATT EVANS.

PROBLEMS OF OLD AGE

Our Advancing Years: An Essay on Modern Problems of Old Age. By T. H. Howell, M.R.C.P.Ed. (Pp. 192; 28 illustrations. 16s.) London: Phoenix House Ltd. 1953.

This essay on the problems of old age is intended to encourage and stimulate our efforts in the medical care of the aged and to focus the attention of the public on their problems and needs. The author has had a wide and prolonged experience in the care of the aged and chronic sick, and this sensitively written book is welcomed as a record of his findings and his philosophy. The keynote here is the assistance of people in their search for happiness in old age. The author wisely points out that "happiness in elderly people is more closely associated with their psychological condition than their bodily health." This is a simple and profound truth applicable to all of us. The author suggests that in the aged, on the whole, cancer does not cause a great deal of pain. It is to be hoped that this is true, and, if indeed it is, the more widely this truth is known the happier many people will be. La Rochefoucauld is quoted: "Old age is a tyrant who forbids all the pleasures of youth, under pain of death"; to which some who are happily growing old might reply that they are well content.

Dr. Howell notes with approval that one London teaching hospital has broken with tradition and has established a geriatric unit. He would perform a valuable service if he could persuade all the other teaching hospitals to do likewise—perhaps this book may assist in their enlightenment.

There is but one small criticism. Dr. Howell with characteristic diffidence apologizes for mentioning by name some of his colleagues in geriatric practice. He is clearly right to discuss them and their work, but perhaps it would have been better to omit the adulatory adjectives. The superlatives, if any, are best left to after-dinner speakers, movers of votes of thanks, book reviewers, and writers of obituary notices.

This is a good book and worthy of careful study by everyone who is or may be concerned with the care of the aged and chronic sick—and that embraces everyone.

C. METCALFE BROWN.

INTRODUCTION TO OPHTHALMOLOGY

Parsons' Diseases of the Eye. By Sir Stewart Duke-Elder, K.C.V.O., Ph.D., D.Sc., LL.D., M.D., F.R.C.S., F.A.C.S. 12th edition. (Pp. 606; 22 coloured plates and 465 text figures. 42s.) London: J. and A. Churchill. 1954.

This is the best introduction to ophthalmology in English, and its value has been increased by changes made since the previous edition. Useful facts about modern therapy have been assembled in Chapter 10, and the new illustrations are excellent. Although rare conditions cannot all find room, many have been briefly surveyed. Moreover, Sir Stewart has helpfully described topics of recent interest, including

maternal rubella, toxoplasmosis, retrolental fibroplasia, and corneal grafting. How could so much new material be inserted without enlarging the book? Expert production gives the answer. The type is closer, and many paragraphs are set small. Publishers and printers deserve praise for arranging more words in fewer pages without sacrificing legibility, and the spacing of illustrations is vastly improved.

Certain treatments recommended for conjunctivitis and blepharitis are old-fashioned. Few would advise daily lid-painting with silver nitrate (p. 137) for gonococcal conjunctivitis. Bicarbonate of soda (p. 522) is inferior to hydrogen peroxide for removal of lid-crusts, and aniline dye painting is more effective than inunction of mercury in blepharitis. Haloes (p. 235) are not pathognomonic of glaucoma, and is it true that prophylactic iridectomy on a quiet eye (p. 241) "invariably results in a complete cessation of the disease"? Greeves's operation for ptosis, commended on p. 535, often produces gross hypertropia. On p. 473 Fig. 383 correctly indicates that the right superior rectus and left inferior oblique are the muscles chiefly concerned in looking up and to the right, but the text does not tally. Just below Fig. 383 the words *ad*ducted and *ab*ducted should be transposed; and in the next sentence the relevant muscles should be the *right* superior rectus and the *left* inferior oblique.

These defects are mentioned because the book's merits transcend them. Chapters 18 and 19, on fundus abnormality, abound in clinical wisdom, but young ophthalmologists should read the whole book six times to get acquainted with their subject. Thus will they learn to profit from larger books, of which Sir Stewart's six-volume system is easily the best.

J. H. DOGGART.

VITAMINS

The Vitamins in Medicine. By Franklin Bicknell, D.M., M.R.C.P., and Frederick Prescott, M.Sc., Ph.D., F.R.I.C., M.R.C.P. 3rd edition, revised and enlarged. (Pp. 784; 245 figures. 70s.) London: William Heinemann Medical Books. 1953.

The 11 years which have elapsed since the appearance of the first edition of this valuable book have seen great advances in our knowledge of many of the vitamins. In preparing its third edition Drs. Bicknell and Prescott have kept in step with this progress, both in describing new discoveries and in removing from their text references to work which has failed to stand the test of time. Their claim that their labours amounted to little short of complete rewriting can be accepted without question. Our gratitude and congratulations are due for the high standards which they have maintained, both in literary presentation and in the accuracy of their statements, in a volume which includes over 5,000 references to sources of information and nearly 250 illustrations.

As in previous editions, each vitamin has been considered under the headings of history, chemistry, sources, physiology, pharmacology, human requirements, deficiency diseases, methods used for detecting deficiency, and clinical applications. The emphasis is on human rather than on animal aspects, but experiments on animals which have a bearing on human vitamin requirements receive adequate mention. The chemistry and biochemistry of the vitamins and the details of their significance in medicine have seldom been so ably and clearly treated in the same book. As an aid to the diagnosis of vitamin deficiencies the clinician can refer to an excellent collection of photographs, which often show the appearance of the same patient before and after treatment with the appropriate vitamin.

The industry and understanding with which the authors have recorded the progress of research on every vitamin deserve high praise. Their obvious determination that nothing of importance should be missed out, however, may bring some risk of questionable material being included. The specialist in nutrition, and doubtless the authors themselves, will have no difficulty in distinguishing between established facts and claims still requiring confirmation, but the general practitioner may find it less easy to discriminate. Thus, an excellent chapter on vitamin P, which is claimed to be necessary for the control of capillary fragility, does not perhaps sufficiently emphasize that many authorities would resist the classification of substances having this activity as vitamins. Similarly the cautious account of the possible significance of vitamin-E deficiency in the aetiology of human muscular dystrophy might give rise to some confusion between speculation and fact in a less cautious reader. However, we must congratulate the authors on producing a book which will serve the clinician well when he is confronted with patients in whom vitamin deficiency may be suspected.

T. MOORE.

ADRENOCORTICAL STEROIDS

Ciba Foundation Colloquia on Endocrinology, Volume VII: Synthesis and Metabolism of Adrenocortical Steroids. Consulting editor for this volume, W. Klyne, M.A., B.Sc., Ph.D. General editor, G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., assisted by Margaret P. Cameron, M.A., A.B.L.S. (Pp. 297; 375 structural formulae and 27 illustrations. 30s.) London: J. and A. Churchill. 1953.

This volume follows the same general form as its predecessors in this series and maintains the same high standard. It reports the proceedings of two conferences.

The first, on synthesis of adrenocortical and related steroids, has a largely chemical emphasis. One section on substances present in cholesterol includes an account of lathosterol. Another describes briefly the synthesis of adrenal cortical hormones from ergosterol, and a further one on cortisone production from sarmentogenin includes an account of the distribution of this raw material in Africa. Other sections describe the synthesis of 11-oxygenated steroids from ergosterol, the infra-red spectroscopy of trisubstituted steroidal olefines, the stereochemistry of C-20, and the effects of *x* rays on steroids.

In the second conference the emphasis is on biochemistry. In a review of adrenal perfusion work at the Worcester Foundation an account is given of attempts to produce C^{14}-labelled compound F. A.C.T.H. is shown to increase formation of compounds B and F from C^{14}-labelled cholesterol. Studies of the enzymes involved in the synthesis and breakdown of adrenal hormones have analysed specially the oxidation of 3β hydroxy-steroids to $\alpha\beta$ unsaturated ketones. Separate enzyme systems for hydroxylation at 11, 17, and 21 positions seem to exist, and the substrate requirements of some of these are outlined. Species differences in adrenal secretion are reviewed and some data are given on the new adrenal hormone influencing salt excretion and now called electrocortin. A section on corticosteroid metabolism in man reveals that some 33 "corticoids" can be found in urine and about 40 in human adrenal gland perfusates. A polarigraphic method is offered for estimating some of these steroids in blood.

The field of steroid metabolism has already become so complex that few can follow all its developments. The present volume should help workers in one field to learn what fellow workers in neighbouring fields of steroid work are doing and thinking.

C. L. COPE.

Dr. Henry E. Sigerist's *Grosse Ärzte* first appeared in 1932, to be followed by an English translation in 1933. It contained biographical sketches of fifty-five of the most important men in medical history, ranging from Imhotep to Osler. Written against a background of knowledge acquired during a lifetime devoted to the study of the history of medicine, the book was recognized as a major contribution to medical biography. A new German edition has now been published (J. F. Lehmanns Verlag, Paul-Heyse-Str. 26, Munich 15, price DM.24), in which Dr. Sigerist has taken the opportunity to revise his work in the light of further information that has come to hand during the past twenty years. He has also added five new biographies (Ramón y Cajal, Pavlov, Cushing, Friedrich von Müller, and Sauerbruch). Excellent portraits round off this finely produced volume, and it is to be hoped that a new English translation will soon be available for those whose unfamiliarity with German prevents their full enjoyment of a delightful book.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY MARCH 6 1954

CHILD LIFE AND HEALTH

No higher tribute could be paid to the child welfare services than that contained in Professor Charles McNeil's Fleming Memorial Lecture, reproduced in the opening pages of this issue. McNeil is of the opinion that success in the promotion of health in childhood in the future rests with the child welfare services, and he submits a plea for a strengthening of the services by providing what he terms "new and better weapons." His views differ from those expressed by Professor A. L. Banks,[1] who suggested that the maternity and child welfare service had largely accomplished its intended purpose and could now be merged with the hospital and paediatric services. It is, incidentally, remarkable that it is the hospital physician who advocates strengthening of the maternity and child welfare service, while the former public health officer recommends its demobilization. These two opposing, and perhaps somewhat extreme, views have in common that they contain little reference to the school health service and to the importance of the family doctor. If, as McNeil emphasizes, it is by education of the mother that child care can best be promoted, what more appropriate place could there be to do so than in the home? And if that be so, has the family doctor no part to play? It is no uncommon experience to hear it said that the general practitioner is not interested in prevention. There may be some foundation for the statement as a generalization. None the less, much of the work of many family doctors is concerned both directly and indirectly with the prevention of disease and with the promotion of health among the children in their practices. Not a few general practitioners give part-time service in local authority clinics. Others have their own organized arrangements specifically intended to cater for the needs of the expectant and the nursing mother and of the infant and child: this trend is one which will almost certainly be favoured by the encouragement being given to group practice. Evidence in some areas suggests that these arrangements are stimulating requests for the periodic examination of 3- and 4-year-old children whose mothers have stopped bringing them to the welfare clinics.

[1] *British Medical Journal*, 1952, 2, 1007.

The family doctor possesses numerous and in many ways unique opportunities to educate parents in child care. (Professor McNeil writes mainly about the education of mothers, but should not fathers have a share of the instruction?) While it is true to say that in the past the general practitioner has not on the whole received very much encouragement in this field, it must be admitted that his attitude has not always invited encouragement. The crux of the present problem is this: Is the family doctor capable of utilizing his opportunities to educate parents, and, if he is, will he find himself in conflict with the statutory child health services? In answering these questions account must be taken of the changes brought about within recent years in the instruction given the medical student in paediatrics and child health. The basis of instruction is the study of health. The student sees the child at home, in the nursery, in the residential home, at the welfare clinic, and in school; and he has opportunities of observing the day-to-day work of the medical and nursing staff of the child welfare and school health services among children, and also the family doctor's work. It is against this background that the student is encouraged to study disease, the restoration of well-being, and the promotion of healthy growth and development. There is already evidence that the young doctor enters practice suitably equipped and anxious to co-operate with the child health services in their work of education. Further progress in this direction would be discouraged, not favoured, by merging the child welfare services with the hospital obstetric and paediatric services. The foundations of child life are in the home. The success of measures to improve child health depends on acceptance of this conception. Sanitation has improved out of all bounds; so also have the general standards among children of cleanliness, clothing, and nutrition. In contrast, despite great improvements, housing and overcrowding remain the most potent deterrents to a nation-wide attainment of optimum health in childhood.

Hospital management committees intent upon making provision for the sick are not always successful in interpreting the special requirements of the ailing child and cannot be expected fully to understand the needs or methods of parental education in child health, which should not be weighted in favour of hospital or specialist considerations. The need is for an increasingly close link between the general practitioner and the children's services provided by the local health authorities. With education for child health there might well be combined education in the care of childhood ailments, if only to reduce the number of unnecessary references of children to hospital

and to foster in mothers a confidence in their own ability to tend their sick children. Centres of study and schools of training in child health along the lines advocated by Professor McNeil would serve to co-ordinate the activities of all those working in this field, and would, as he believes, add to the authority and prestige of the child welfare service.

Q FEVER

When Q fever was first recognized in 1937[1] it appeared to be mainly an occupational disease affecting slaughter-house workers and restricted to the vicinity of Brisbane. This idea of the disease changed notably during the 1939–45 war, when it was established that several outbreaks of non-bacterial or atypical pneumonia in Allied and enemy forces in Southern Europe were caused by infection with *R. burneti*, the causative agent of Q fever.[2 3] Subsequent reports, in addition to confirming the unusual feature of pulmonary involvement seen in man, have drawn attention also to the world-wide distribution of Q fever in animals.[4 5]

Although a rickettsial disease, Q fever differs in many respects from the rest of this group of infections. Insect vectors, for instance, play little or no part in the spread of the disease to man, and the part they play in transmission of the disease from animal to animal is by no means an essential one. Cutaneous rashes are uncommon, and serum agglutinins to the proteus group do not appear in the patient's blood. Indeed, one of the few findings in Q fever, in common with other rickettsial infections, is the severe headache so frequently present. It now seems well established that infected animals—cows, sheep, and goats in particular—are the main sources of human infection. The organism is excreted in the faeces, the placenta, and the milk of infected animals, and infection is by inhalation of infected excreta or by drinking contaminated milk.[5] *R. burneti* is a hardy organism, being relatively resistant to inactivation by normal physical and chemical methods. Pasteurization is only just adequate to inactivate the organism if the correct conditions are scrupulously maintained.[6]

The presence of Q fever in Britain was established in 1949,[7] since when both outbreaks and sporadic cases have been reported.[8 9] So far cattle appear to be the only reservoir of infection in this country.[9] A recent survey of Q fever in Britain by Marmion and his colleagues[8] shows that a large proportion of the observed cases have occurred in the south-eastern counties, where a corresponding higher proportion of infected cattle have also been found. Epidemic Q fever as seen in Italy in 1943–4 is not likely to cause much confusion in diagnosis, but considerable variation is seen from case to case, and asymptomatic infection is by no means uncommon. Harman,[10] reviewing the clinical features, emphasizes that some of the points in favour of a diagnosis of Q fever are the extremely sudden onset, severe headache, often out of all proportion to the severity of the case, and the lack of upper respiratory or gastro-intestinal symptoms. Later an unproductive cough and radiological evidence of pulmonary infection develop. Serological tests are useful in helping to distinguish Q fever, and in particular the mild or sporadic case, from other forms of pyrexia of unknown origin labelled as influenza or atypical pneumonia. Specific antibodies can be detected by the seventh to twelfth day by the complement-fixation test, which remains positive for a considerable time.[11 12] Except in old people the prognosis is good, with full recovery in most cases, but there is the possibility that some cases may become chronic and prove resistant to antibiotic treatment.[9] Fortunately Q fever is not a serious problem in this country, but as the risk of milk-borne infection exists it would seem advisable on general principles to reduce the risk by suitable treatment of raw milk.

MEASURING HOSPITAL EFFICIENCY

The efficient use of the available hospital beds in this country is of special importance because of the meagre allocation of money for building new hospitals and major hospital extensions. When considering the use being made of the existing hospital beds, discussion is apt to centre on certain statistical information, and in particular on bed occupancy rates. Avery Jones[1] believes that a general community hospital should have at least a 90% bed occupancy and that it is feasible to achieve a 93% bed occupancy. The fact that there are many hospitals up and down the country with only 80% bed occupancy, and some substantially lower, he considers to be evidence of extravagance, and he concludes that, on the basis of the bed occupancy figures reported, there cannot be said to be any overall shortage of hospital beds in this country.

In assessing the amount of hospital accommodation required, and the efficiency of a particular hospital,

[1] Derrick, E. H., *Med. J. Aust.*, 1937, **2**, 281.
[2] Robbins, F. C., and Ragan, C. A., *Amer. J. Hyg.*, 1946, **44**, 6.
[3] Caughey, J. E., and Dudgeon, J. A., *British Medical Journal*, 1947, **2**, 684.
[4] Berge, T. A., and Lennette, E. H., *Amer. J. Hyg.*, 1953, **57**, 125.
[5] Babudieri, B., *W.H.O. Monograph Series*, No. 19, 157. 1953.
[6] Stoker, M. P. G., *Brit. med. Bull.*, 1953, **9**, 231.
[7] —— *Lancet*, 1949, **1**, 178.
[8] Marmion, B. P., and Stoker, M. P. G., ibid., 1950, **2**, 611.
[9] —— *et al.*, ibid., 1953, **1**, 503.
[10] Harman, J. B., ibid., 1949, **2**, 1028.
[11] Kaplan, M. M., and Hulse, E. C., *W.H.O. Monograph Series*, No. 19, 175. 1953.
[12] Babudieri, B., ibid., 193. 1953.

considerations other than mere figures must be given due weight, though statistical data are essential if the questions are to be fully studied. But the figure of bed occupancy is only one index of efficient bed utilization, and others must be taken into account, such as the average length of stay of patients in the hospital concerned and the "turnover interval." This is the interval which elapses between the discharge of one patient and the admission of another into the same bed. If the bed occupancy figure alone were taken into account in assessing the full utilization of a particular hospital bed, then the figure of 100% bed occupancy could be obtained by keeping one patient throughout the year in that bed. In other words, by increasing the length of stay and reducing the number of patients occupying the bed in one year, the bed occupancy rate will rise, but it cannot be said that the bed has necessarily been efficiently utilized. A hospital which has a low figure for the average length of stay, a minimum turnover interval, and a high bed occupancy rate is statistically a much more efficient hospital than one which has a high static bed occupancy. When these three requirements have been achieved, considerably more patients are being treated in the same number of hospital beds during a given period. As an example of the measurement of this kind of efficiency the figures for the Manchester Region may be taken. There, 20,000 more in-patients were dealt with in 1951 than in 1950 without any increase in the actual number of hospital beds. The alternative to this increase in the turnover would have been to provide a new hospital of 800 beds.

When considering bed utilization, the number of patients who have occupied the beds during the year must therefore be taken into account in addition to the percentage bed occupancy. This figure, known as the bed turnover or bed-use factor, is calculated by dividing the number of patients who were discharged or died during the year by the number of available beds. In the report of the Chief Medical Officer of the Ministry of Health for 1952[2] it is shown that there is considerable variation in this figure for hospitals which prima facie appear comparable. For example, the average figure for the London undergraduate teaching hospitals for 1952 in general medicine was 12.3 and that for provincial undergraduate teaching hospitals was 19.1, while the corresponding figures for general surgery were 19.4 and 25.0 respectively. Because of these wide variations, the bed occupancy rate taken in isolation can be misleading, for a higher figure of bed occupancy will be obtained in the hospitals with a longer duration of stay if the turnover interval remains the same. Murley[3] has pointed out that an increase in turnover will result in a lower bed occupancy figure, but this is conditional on the turnover interval remaining constant. At present the national figure for the turnover interval is 3.26 days, but there must be a minimum level to which the turnover interval can fall, and when this is reached improved utilization can be effected only by reducing the length of stay, which in turn reduces the rate of bed occupancy. At this point a rise in bed occupancy would in fact indicate that beds were being less efficiently used.

All these indices, therefore, have to be taken into account in considering the use of available hospital beds from a statistical point of view, but even so allowance must be made for the great variety of circumstances in different hospitals. In an acute general hospital it is not possible to obtain a 100% bed occupancy except by crowding in extra beds above the normal bed complement, particularly when wards have to be reserved for separate groups —for example, maternity patients. Indeed, it is undesirable for an acute general hospital to have a 100% bed occupancy, otherwise no reserve beds would be available for the admission of emergency cases. The admission of day cases for operation, variations in bed allocations to individual specialties, differences in hospital requirements in an industrial area as compared with a residential area, and the shortage of ancillary facilities in a hospital will all affect the bed occupancy figure, making it inappropriate for use as the sole yardstick for comparing hospitals of the same size and apparently otherwise comparable. But it can be a useful guide to hospital staffs and administrators in assessing the use which is being made of available resources when taken in conjunction with other factors and over a suitable time.

[1] *Lancet*, 1953, 1, 999.
[2] *Annual Report of the Chief Medical Officer of the Ministry of Health*. H.M.S.O. 1952.
[3] *Lancet*, 1953, 1, 1153.

CANCER REGISTRATION

The development in Britain of cancer recording on a national scale comparable with the Danish system has been beset with difficulties. The Radium Commission, which controlled the supply of radium from 1930 to 1948, was in the fortunate position of being able to insist on the keeping of records wherever radium was used, but the obligation applied only for patients treated by radiotherapy, and it had to be suspended during the war and lapsed altogether in 1948 with the National Health Service Act. In 1939 the Ministry of Health had advised county and county borough councils to provide for the keeping of records of treatment and its results as part of the plans asked for under the Cancer Act, and in 1944 a circular letter was issued on

the subject. The Radium Commission, having devoted much attention to methods of recording, introduced a standard card for use in radiotherapy centres, and in 1947 the General Register Office became the statistical bureau for dealing with the cards. After the repeal of the Cancer Act in 1948 local responsibility for cancer registration passed to the regional hospital boards and teaching hospitals, but not all have acted.

In 1945 some 29,000 cancer cases were registered, and by 1948 the annual number had risen to about 49,000, not yet amounting to half of the estimated total of new cases seen annually in England and Wales, and not properly representative because of overweighting with radiotherapy patients. In the first report issued by the General Register Office[1] the cases registered in 1945 and 1946 were studied with one-year survival rates, these being supplemented later by rates of survival to two and three years.[2] In a further supplement[3] recently published the 1947–8 registrations have been analysed for each cancer site by sex, age, and confirmation of diagnosis, and also by interval before treatment at each hospital centre.

Since 1948 little further progress has been made towards reaching the objective of complete cancer registration, and it is to be hoped that a circular[4] just issued by the Ministry of Health to regional hospital boards will receive serious attention. It expresses concern at the slow progress and underlines a recommendation of the Minister's Standing Advisory Committee on Cancer and Radiotherapy that registration should be continued on a voluntary basis in all regions, using a simpler follow-up card which has been designed by a special subcommittee of the Registrar-General's Advisory Committee on Medical Nomenclature and Statistics. In revising the standard card great care was taken to eliminate items which experience has shown to be of doubtful value or to present difficulty, and the new abstract card can easily be transcribed by a lay clerk from clinical records. Brought up to date and shorn of resemblance to an official record form, it aims to provide essential information on cancer incidence by site, sex, age, geographical area, interval between first signs and start of treatment, methods of treatment in use, and survival according to extent of disease when first seen. Regional hospital boards are asked to examine the position in their regions in conjunction with the teaching hospitals and to report by June 30 on the projected development of cancer registration.

In some regions the teaching hospitals have shown little enthusiasm for cancer recording, and in others discouragement has been felt because of lack of publication of findings as they concern the region. The United Birmingham Hospitals set a good example by deciding to issue a series of annual reports on survival of cancer patients admitted during the period 1936–49. The first[5] of the series deals with the methods of treatment and survivals to two and five years of some 6,500 patients with new growths of the alimentary tract and tongue. This report is a model of concise presentation, profusely illustrated by 32 diagrams, and, depressing though many of the facts recorded undoubtedly are, their presentation in a manner such as this can do nothing but good. It is much to be desired that other hospital regions will strive to bring their cancer registration nearer to completeness with a view not only to providing the national information that is needed but also to producing regional studies of this kind on special aspects of the cancer problem.

[1] "Cancer Registration in England and Wales," *Studies on Medical and Population Subjects*, No. 3, 1950, General Register Office.
[2] Supplement to above, 1952.
[3] *Registrar General's Statistical Review for 1949*, Supplement on "General Morbidity, Cancer and Mental Health," 1953.
[4] H.M. (54) 18.
[5] Annual Cancer Report of the United Birmingham Hospitals, Vol. 1, 1953.

BURNS AND THE ADRENAL

The weak point in all discussions on stress and the pituitary–adrenal axis is the gross inadequacy of all the methods of assessing the activity of the adrenal cortex, whether in the experimental animal, the live patient, or even at post-mortem examination. Without exact and objective evidence on this point the way lies open to the flood of hypotheses which have swamped and almost discredited this most important field of research. Reliable methods for chemical assay of steroid hormones in the blood are the only final answer, and are slow in appearing. Meanwhile modern histochemical techniques are being used in a promising new attack[1] on the problem of estimating pituitary and adrenal activity from examination of post-mortem specimens; and, as Dr. S. Sevitt shows elsewhere in this issue, the only technically simple method of approach—the eosinophil count—can still give useful results in a field which has become the province of the well-equipped biochemist. In 1951 Dr. Sevitt[2] described the changes in the eosinophil count in burned patients seen at the Birmingham Burns Unit. The eosinophils fall from their normal 200 per c.mm. to below 40 within two hours of the accident and remain low for several days.[2 3 4] The period of eosinopenia can be presumed to correspond to a period of increased secretion of cortical steroids. Broadly speaking, the duration of the eosinopenia depends on the severity of the injury, being a day or less in burns involving 10% of the body surface, and four to five days in 50% burns. A moderate "rebound" eosinophilia often follows.

Some patients show less eosinopenia than would be expected from the size of their burns, as Sevitt and others[4] have found, and this seems to worsen the prognosis. An inadequate adrenal response to stress is the obvious suggestion. Sevitt's present work offers new evidence of this and gives some indication of its causation. The eosinophil responses were studied in burned patients who had passed the initial eosinopenic phase. Two drugs were used which have different mechanisms. A.C.T.H. acts directly on the adrenal, and failure to respond to it indicates an unresponsive adrenal. Intravenous adrenaline acts on the pituitary (perhaps through the hypothalamus), stimulating the production of

[1] Symington, T., and Currie, A. R. Papers read to the Pathological Society at Birmingham in January, 1954.
[2] *British Medical Journal*, 1951, 1, 976.
[3] Evans, E. I., and Butterfield, W. J. H., *Ann. Surg.*, 1951, 134, 588.
[4] Wight, A., Raker, J. W., Merrington, W. R., and Cope, O., ibid., 1953, 137, 175.

A.C.T.H. A patient who responds to A.C.T.H. but not to adrenaline must have some defect at the pituitary end of the axis. Two of Sevitt's patients failed to respond to A.C.T.H., and one of these died: though equivocal, the post-mortem findings were compatible with true adrenal cortical failure. Three other patients were found in whom intravenous adrenaline was ineffective: two had simultaneous mental changes, and the suggestion that a hypothalamic lesion was present seems reasonable. Sevitt has established the fact that adrenal cortical deficiency can occur in burns, and that at least two wholly distinct mechanisms can be involved. It follows from his work that there is a case for treating some (not more than 10%) of burned patients with cortisone for short periods.

EMOTIONS AND THE NOSE

The primary purposes of the nose are olfaction and conditioning of the air which passes through it, so that when the air reaches the lower respiratory tract it will be suitably filtered, warmed, and moistened. This conditioning of the inspired air includes the filtering-off of unwanted foreign particles and the giving-off of more than a litre of moisture in the course of 24 hours. Such activity is made possible by the nasal mucous membrane, which is rich in blood vessels and mucous glands. The surface area of the nasal mucous membrane is also greatly increased by the turbinals, which project into the nasal cavities and contain erectile tissue enabling them to swell and give off mucus in accordance with the needs of the body. This delicate mechanism is under the control of the parasympathetic system and can be readily invoked by a variety of stimuli, some of which may be quite unconnected with respiration. Nasal obstruction and hypersecretion are part of many emotional experiences—the "honeymoon cold," for instance, being a common phenomenon. Holmes, Goodell, Wolf, and Wolff,[1] in a study of reactions within the nose in human subjects during varying emotional situations, have continued observations which they had previously made by direct observation of the mucosa of the stomach in a patient with a large gastric fistula. They found that circulatory changes in the nose were similar to those in the gastric mucosa. In particular they noted that emotional reactions induced by anxiety, resentment, and feelings of frustration were associated with hyperaemia and hypersecretion in both nasal and gastric mucosae. They concluded that if such reactions were sustained troublesome symptoms would result which might predispose to chronic disease in the nose.

Elsewhere in this issue Mr. P. Reading, Mr. K. Malcomson, and Mr. D. O'Neill give an interesting account of the investigation and treatment of chronic vasomotor rhinitis. When hay fever is excluded they found that there is still a large and troublesome group of sufferers in whom inhaled allergens play little part in the aetiology. These workers believe that chronic vasomotor rhinitis is a disorder associated with emotional tension or stress and is therefore comparable in aetiology with asthma and duodenal ulcer, in which the cholinergic system seems to play a part. When local and general treatment failed to alleviate the rhinitis, psychological investigation often brought to light a condition of emotional strain, and psychotherapy, sometimes continued for 20 months, had a gratifying success in relieving both paroxysmal rhinorrhoea and chronic nasal oedema.

[1] *The Nose*, 1950, Springfield, Illinois.

FOLIC ACID AND PERNICIOUS ANAEMIA

The Addisonian type of macrocytic anaemia is effectively treated with extracts of liver or stomach or with vitamin B_{12} (cyanocobalamine); on the other hand, hypochromic microcytic anaemia responds only to full doses of suitably administered iron preparations and neither requires nor responds to the other anti-pernicious-anaemia agents. Nevertheless, in spite of these simple therapeutic facts, many elegant and expensive preparations containing iron, vitamins, liver and stomach extracts, yeast, copper, vitamin B_{12}, folic acid, and often other substances, are on the market and recommended by their manufacturers to the doctor for the treatment of his anaemic patients. These polypharmaceutical remedies rarely contain enough of any constituent to deal effectively with any form of anaemia, while their heavy cost sometimes leads the doctor to prescribe them in such small doses as one pill or capsule per day. Anaemic patients still commonly receive some form of treatment with these blunderbuss preparations before their blood has been examined for the purpose of determining the type of anaemia and the appropriate treatment. Then, when a patient does not fully respond to the remedy given, subsequent blood and marrow examinations may fail to give a clear-cut diagnosis. This difficulty is noticed most often in pernicious anaemia—which is still a fatal condition if not properly treated—since the bone marrow rapidly loses its megaloblastic character even after inadequate anti-anaemic treatment, though this does not necessarily lead to a remission of the anaemic state.

Elsewhere in this issue Dr. C. P. Lowther (p. 564) once again draws attention to the dangers of this practice. In the past the worst that could happen to a patient with pernicious anaemia treated with an ineffective remedy was a failure to respond to treatment, the development of a more severely anaemic state, and, consequently, a misdiagnosis of refractory macrocytic anaemia; usually, and fortunately for the patient, this led to subsequent reference to hospital for investigation, diagnosis, and treatment. Now, however, the danger is more serious and may be acute, because so many of the blunderbuss anti-anaemic preparations contain folic acid, though this is not always realized by those who prescribe them. The tablets taken by Dr. Lowther's patient contained this substance. Both Davidson[1] and Wilkinson[2] clearly showed that folic acid was undesirable for the treatment of pernicious anaemia, while in 1949 Israëls and Wilkinson,[3] and others, later concluded that folic acid induces peripheral

[1] *Edinb. med. J.*, 1948, **55** 400.
[2] *British Medical Journal*, 1948, **1**, 771, 822.
[3] Ibid., 1949, **2** 1072.

neuritis and spinal cord degeneration in patients with pernicious anaemia who had previously shown no signs of such complications, or else makes worse an early peripheral neuritis. The onset of such, often acute, neurological complications may be quite sudden, and in some cases even while liver extracts or vitamin B_{12} are being given at the same time as folic acid, as was the case with Dr. Lowther's patient, who had been taking 3 mg. of folic acid daily for only 38 days. Fortunately, if the real diagnosis is made early enough, the prompt administration of liver extracts or vitamin B_{12} and the immediate discontinuance of the folic acid usually reverses this disconcerting and serious complication.

Folic acid has no place in the treatment of pernicious anaemia and is of no value in hypochromic microcytic anaemia. In patients with pernicious anaemia it may mask the development of, or deterioration in, neurological symptoms by bringing about a false sense of improvement in the general symptoms and a variable degree of improvement in the blood count. There is now a strong case against the inclusion of folic acid in polypharmaceutical anti-anaemic preparations, the usefulness of which in the opinion of most haematologists is in any case open to grave doubt.

PYRAZINAMIDE WITH ISONIAZID IN TUBERCULOSIS

Drugs in bewildering variety, falling into several main classes, are now known to possess anti-tuberculous activity, and their use in various combinations and for different forms of the disease bid fair to occupy the attention of investigators for some years to come. One of the latest and least familiar is pyrazinamide ("aldinamide"). This is a derivative of nicotinic acid, as isoniazid is of isonicotinic acid, and was shown to exert moderate anti-tuberculous activity in guinea-pigs by Dessau and his colleagues.[1] In a clinical study[2] they reported on the treatment of 43 patients, of whom 25 had far advanced disease: the results were generally encouraging, although the authors regarded the usefulness of the drug as limited by the rapid emergence of drug-resistant bacilli, particularly in patients with far advanced tuberculosis with large cavities.

Walsh McDermott and his colleagues[3] now report a clinical study of the action of pyrazinamide and isoniazid given together, prefaced by a description of an animal study by McCune and Tompsett of which a fuller account is to appear later. The latter workers used this drug combination in infected mice, and studied its effects by quantitative cultures of the organs. The striking fact which emerged was that the initial fall in the bacillary content of the spleen which follows the use of either drug alone or of other forms of chemotherapy was continued during combined treatment to complete extinction. This apparent sterilization of splenic lesions has never been achieved before, and suggests an "eradicative" action in surprising contrast to the relative inactivity of pyrazinamide *in vitro*. The clinical study embraced 81 patients, of whom some were treated in New York City and some (presumably Navajo Indians) in the Navajo Medical Centre, Fort Defiance, Arizona. In all but nine the pulmonary lesions were classified as far or moderately advanced. Both drugs were given orally, pyrazinamide in a daily dose of 50 mg./kg. and isoniazid in one of 5 mg./kg., the intention being to continue this treatment for three months and to continue thereafter with isoniazid alone: complete courses were given to 61 patients, early deaths and other causes having prevented completion in the remainder.

The results from all points of view but one were gratifying. An effect comparable to that observed in the mouse spleen was apparently obtained in the disappearance of bacilli from the sputum of 90% of the patients. Substantial radiographic improvement was achieved in 70% and cavity closure in 65% of those with cavitation. On the other hand, unequivocal signs of liver damage developed in six patients, and this complication was fatal in one of them. Jaundice with impairment of liver function was also observed by Yeager, Munroe, and Dessau[2] in two of their 43 patients. Although this does not mean that the treatment is unjustifiable, it clearly can be used only under strict supervision: its freedom from any tendency to cause gastro-intestinal upset, in contrast with the disturbing effects of P.A.S., had encouraged the hope of domiciliary application. Possibly a modification of dosage may diminish this risk of toxic effect.

[1] *Amer. Rev. Tuberc.*, 1952, **65**, 519.
[2] Ibid., 1952, **65**, 523.
[3] Ibid., 1954, **69**, No. 3.

THE CLARE WAND FUND

The Conference of Local Medical Committees at its meeting on June 26, 1952, resolved to pay a tribute to Dr. S. Wand and Dr. D. P. Stevenson—chairman and secretary of the General Medical Services Committee—in recognition of their "outstanding services to the profession during the negotiations on remuneration which culminated in the Danckwerts award." An appeal was sent to all local medical committees in which it was suggested that the major portion of the money subscribed should be used to form a fund to provide educational assistance for doctors in general practice. At the wish of Dr. Wand the fund was to be called the "Clare Wand Fund." In the first letter in this week's *Supplement*, the chairman of the Trustees of the Fund puts forward tentative proposals for the use of the sum of £12,000 which has been subscribed. Further suggestions, it says, will be sympathetically examined. Some may well be forthcoming, but the Trustees' own ideas seem to be well designed for their purpose of encouraging "projects which will enhance the prestige of general practice."

We announce with regret the death on February 27 of Dr. T. Jenner Hoskin, senior physician and cardiologist to the Royal Free Hospital. A memoir will be published in next week's *Journal*.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

TESTS FOR VENEREAL DISEASE—I

BY

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Laboratory tests for venereal diseases are mostly concerned with gonorrhoea, non-gonococcal urethritis, chancroid (soft sore), and syphilis. Occasionally laboratory investigation of material from patients suspected of suffering from lymphogranuloma inguinale (lymphogranuloma venereum) or granuloma inguinale is required.

At the outset it must be stressed that before instituting treatment for any of these diseases laboratory assistance should always be invoked in order to confirm the diagnosis, and when occasion demands the practitioner should telephone the laboratory for the necessary glass slides, culture media, or screw-capped bottles, with containers for transport. If he is uncertain about which test should be employed, the pathologist will give the necessary advice.

Before taking material from the patient it is essential to mark each specimen with an identification name or number, the date, and the source of the material—for example, urethra, vagina, cervix.

Specimens

No laboratory, whatever resources it may have or however experienced its personnel, can give the best advice when supplied with badly harvested specimens.

Smears.—These should be made with a platinum loop, thinly and evenly spread on the glass slides (mix a drop of sterile water or saline with a drop of the discharge, if necessary), and fixed by moderate heat—that is, the slide should not feel uncomfortably hot when placed on the back of the hand.

Cultures.—Specimens for culture should be taken with a platinum loop or the sterile wool swabs supplied by the laboratory.

Blood.—With adults at least 8 ml. should be obtained by venepuncture. In order to avoid haemolysis, which may vitiate the tests, care should be taken that both needle and syringe are free from water or spirit (wash out with sterile normal saline if necessary). The needle should be removed before transferring the blood to the sterile screw-capped blood bottle, care being taken to use no undue force. In the case of adults or small children with "difficult veins" a guarded safety-razor blade can be used. All except the last ⅛ in. (3 mm.) of one cutting edge is covered with adhesive plaster; a clean-cut nick is inflicted into the surgically cleaned and warmed heel of the patient. If the skin is stretched by the use of the thumb and forefinger of the left hand and the cut made at right angles to the "stretch," the small wound will tend to gape and sufficient blood will usually run into the container (5-ml. bijou screw-capped bottle) held against the skin below the cut. Umbilical cord blood, as will be explained in Part II of this article, is not a suitable specimen to collect.

Cerebrospinal Fluid.—It is, of course, essential that cerebrospinal fluid should not contain any blood.

Serum from Primary Sore.—A capillary tube closed at one end should be used to obtain serum from a suspected syphilitic sore if the presence of *Treponema pallidum* is to be demonstrated. If the sore is covered with a scab, this should be removed, the lesion washed thoroughly with plain tap-water or normal salt solution (soap should not be used), and then dried. The dried surface is gently scarified so as to provoke *slight* bleeding and the exudation of serum. Wipe away the first few drops of exudation, especially if they contain blood, and wait for a clear drop of serum to appear from the depth of the lesion. Gently heat the closed end of the capillary tube and immediately apply the open end to the drop of clear serum, and as the closed heated end cools allow sufficient serum to be drawn up into the tube so that none is present ½ in. (13 mm.) from either end of the tube. The open end is then sealed by heat.

Clinical Details.—Finally, all specimens should be accompanied by a brief note containing the name and address of the doctor, the patient's name or identification mark, the essentials of the clinical history, the probable diagnosis, and the examination required. It cannot be too strongly stated that "slot-machine" laboratory reports are largely a waste of time and money. If the pathologist and clinician do not collaborate, the latter may well be deprived of vital information.

Transport.—The speedy transport of specimens from the patient to the laboratory is of paramount importance. Time is often the essence of a useful investigation. Fluid specimens may deteriorate rapidly after being taken, and thus the examination of such material would be fruitless. For example, the cells in the cerebrospinal fluid begin to disappear within two hours of lumbar puncture, and in 24 hours few, if any, cells can be seen.

Reports.—Reports on the findings of tests for venereal diseases are intended to be regarded only as part of the evidence required in order to make a diagnosis. Thus a report that no gonococci can be found in the smear from a urethral discharge is no proof that the patient is not suffering from gonorrhoea. Further investigation may be required and the final decision must rest with the clinician.

Identification of Gonococci

When the patient is suspected of suffering from gonorrhoea, three types of test should be employed—namely, smears, cultures, and blood tests.

In acute gonorrhoea in the male smears should be made with a platinum loop from urethral discharge after carefully cleaning up the glans penis and meatus with sterile water or saline. In the female, with the patient in the lithotomy position, smears should be made from the urethra, posterior fornix of the vagina, and the cervical canal. In the case of suspected chronic gonorrhoea in the male smears should be made from the prostatic secretion after massage as well as from the early morning discharge obtained from the urethra after the patient has held his water all night. In the female, examination of smears from the urethra, cervical canal, and the rectum should be made. Satisfactory rectal smears cannot be obtained without the aid of a proctoscope, and unless the practitioner is skilled in the use of this instrument he should obtain the advice of an expert. Strands of mucopus on the mucosal wall can often be found (30% cases, C. S. Nicol, personal communication), which on examination may reveal the presence of gonococci.

Most bacteriologists will report that the smears contain Gram-negative intracellular diplococci and/or other organisms such as coliform bacilli, diphtheroid bacilli, or monilia. Further information on the cellular content of the smear will also be given. Polymorphonuclear leucocytes predominate in acute inflammatory conditions, whilst epithelial cells suggest a more chronic infection. Two points must be remembered: (1) that the absence of the relevant organism

is no proof that the patient is not suffering from gonorrhoea, and an examination of another specimen may be indicated; and (2) a report that Gram-negative intracellular organisms morphologically resembling gonococci have been seen will not be accepted in a Court of Law as proof that the patient from whom the specimen came is suffering from gonorrhoea, because other organisms of the Neisseria group may occasionally be present in the genital tract.

In suspected gonorrhoea in the female smears and cultures should be taken just after the menstrual period.

Cultures should be taken immediately after the smears and from the same anatomical sites. Direct inoculation of discharges on to solid media has been largely abandoned in favour of transport media. The sterile cotton-wool swab impregnated with carbon provided by the laboratory should be well rubbed into the discharge and then plunged straight into a bijou bottle containing Stuart's transport medium. The wooden stick is snapped off by pressure against the side of the bottle so that the screw cap can be replaced and tightly screwed up again. Since the success of this transport medium depends on anaerobic conditions, this manœuvre should be carried out with speed and great care taken to check that the screw cap is not loose when the operation is completed. After receipt at the laboratory, the swab is used to inoculate suitable media, incubated in an atmosphere of carbon dioxide and examined after 24 to 48 hours, depending on the amount of growth obtained. Typical pure gonococcal colonies, if present, are picked off, some examined under the microscope, some tested with the oxidase reactions, and some subcultured for testing with sugar reactions. If gonococci are grown the organism can be isolated in pure culture and "sugared" in 80% of such specimens. These are reported as morphologically and culturally gonococci. The 20% which cannot be obtained in pure culture are reported as "presumptive" gonococci, and warrant the institution of anti-gonococcal treatment, provided the history and clinical condition indicate a strong probability that the patient is suffering from gonorrhoea. If there is any doubt consultation with the bacteriologist is indicated.

Gonococcal Complement-fixation Test

The only blood test at present in routine use is the complement-fixation test for gonorrhoea (G.C.F.T.) and reports on this test are given as negative or positive. Positive reactions are quantitated and reported as positive with neat serum or a dilution thereof. A positive reaction is evidence of a gonococcal focus of infection, but in the absence of any supporting evidence the test should be repeated. A negative reaction, however, does not exclude gonorrhoea, because in the early stages of the disease the body may not have had time to elaborate the antibodies detected by the test. The table shows how soon after *exposure* to infection one might expect a positive G.C.F.T. in untreated gonorrhoea.

Time after Exposure	No. of Cases	Percentage with Positive G.C.F.T.
1st week	663	9
2nd ,, ...	491	16
3rd ,, ...	160	34
4th–6th weeks	90	39
7th week	26	50

During the course of treatment of acute gonorrhoea with penicillin the fate of the reaction is as follows: 68% fail to record a positive reaction throughout the course of their illness; 19.2% are positive at first testing before treatment is begun; 6.4% at the end of the first week of treatment; 2.5% at the end of the second week; 0.8% at the end of the third week; and 0.5% at the end of the fourth to eighth weeks. The remaining 2.1% show "oscillating" reactions—that is, on serial testing at intervals the reaction results recorded may be negative, positive, negative, or alternatively positive, negative, positive. This type of serological pattern probably means that the antibody content of the patient's serum is sometimes over and sometimes under the threshold of recognition by the test. In gonorrhoea this process goes on for a relatively short time, until antibody production recedes, and thereafter negative results are recorded.

Of patients who record a positive reaction at the first testing before treatment, approximately 64% may be expected to become negative after treatment within three months, leaving 36% who will become "oscillators" and revert to negative in due course. Of patients who have a negative test when first tested, and subsequently become positive, 60% will have a positive G.C.F.T. before the end of the first week, when in all probability the treatment has not had time to take effect; 24% will become positive before the end of the second week; and the remaining 16% will become positive during the third to eighth weeks. Complications of gonorrhoea are not common, but at least 66% can be expected to show a positive G.C.F.T.

The value of the G.C.F.T. may be summed up as follows: in early acute gonorrhoea its use is limited; it is of value in subacute or chronic gonorrhoea, particularly in the female, when smears may give little or no help initially; it is of definite value in the diagnosis of complications; it is useful in the management of gonorrhoea; it is unwise to ignore a positive test which has been confirmed by retesting.

Non-gonococcal Urethritis

Non-gonococcal urethritis is a most troublesome condition. According to the latest Ministry of Health returns 11,552 men attended public V.D. clinics with this condition in 1952, as compared with 15,510 new cases of gonorrhoea in the male. The cause of the condition is unknown, though it is thought that it may be due to a virus infection or one of the organisms of the Pleuropneumonia group. Laboratory help is therefore entirely confined to negative findings in excluding a diagnosis of gonorrhoea. In the acute stage of the disease smears from the urethral discharge usually reveal the presence of masses of leucocytes but no organisms. Later many lymphocytic cells and contaminants such as staphylococci and diphtheroid bacilli may also be found. In like manner cultures will either fail to grow any organisms or grow only the contaminants. Blood tests for gonorrhoea are always negative.

Chancroid

Laboratory tests in the diagnosis of chancroid are of some value. Smears taken from the sore usually contain a mass of leucocytes plus a variety of contaminating organisms. Occasionally organisms resembling Ducrey's bacilli (small Gram-negative bacilli, characteristically arranged in chains) may be seen. Cultures can be taken into clotted sterile rabbit's blood which has been heated at 55° C. for five minutes. Fresh medium should be used and a bead of discharge is obtained from the base of the ulcer under its undermined edge by means of a platinum loop. The medium is inoculated by the wire being passed several times round the clot so as to ensure even distribution of the inoculum. Two media tubes should be inoculated and examined after 24 to 48 hours. According to Teague and Deibert* if the characteristic chains and tangles of small Gram-negative bacilli are found even in admixture with contaminants the culture may be regarded with confidence as being positive for Ducrey's bacillus. In all cases a cutaneous skin test (dmelcos) should be performed to confirm the diagnosis and standard serum tests should be requested with a view to excluding syphilis. Always remember that the first result of the latter may be negative if the blood is taken during the incubation period of syphilis.

[*Part II will appear in our next issue.*]

**System of Bacteriology*, 2, 415. Medical Research Council, 1929.

Nova et Vetera

THE JENNER OF AMERICA: A BICENTENARY

Benjamin Waterhouse was essentially and aggressively American—even to the extent of placing after his name on the matriculation roll of the University of Leyden the words *Liberae Reipublicae Americanae Foederatae Civis* in 1778. He came there, as he said, to acquire "a little of the Dutch phlegm." But, ardent nationalist as he was, he nevertheless lived on to illustrate the truth that political ties, however severed, cannot prevent the permeation of scientific thought from one country to another.

Perhaps his English ancestry helped. Born on March 4, 1754, at Newport, Rhode Island, his mother was a cousin of the Quaker physician John Fothergill, F.R.S., collector of one of the finest botanical gardens in Europe and a great friend of Benjamin Franklin. It was with Fothergill in London that he came to study in the year before the Declaration of Independence, and three years later (varied by nine months in Edinburgh) he moved to Leyden. London, Edinburgh, and Leyden fashioned him so well that a year after he returned to America he was offered, and accepted, the chair of physic in the newly founded medical department at Harvard. Here his most immediate colleague was John Warren, the professor of anatomy and surgery, who was reputed to have taken part in the Boston Tea Party, and who had drafted the plans for the medical department. Warren was a bold and skilful surgeon who had not only performed one of the first abdominal operations recorded in America but also pioneered in amputation at the shoulder-joint. It was Warren's clear outlook, no less than Waterhouse's own English connexions, which were to play so decisive a part in the great event which is for ever associated with the name of Benjamin Waterhouse in medical history—the introduction of vaccination into the United States.

It is hard now to estimate the one-time ravages of smallpox. John Coakley Lettsom, a Quaker like Waterhouse and Fothergill, co-operated in reporting to the House of Commons that it was responsible for the loss, in England, of from 34,000 to 36,000 lives annually. No less severe were its ravages in the United States, for as early as 1721, during the sixth epidemic in Boston, Zabdiel Boylston had courageously inoculated his son and two negro slaves and some 244 other persons, risking death by hanging in doing so. Fifty-seven years later, in the same place, a subsequent epidemic led John Warren to establish a hospital. So when Lettsom sent Waterhouse a copy of Edward Jenner's *Inquiry into the Causes and Effects of the Variolae Vaccinae* early in 1799 the immense advantage of cowpox vaccinations over smallpox inoculations was immediately appreciated by Waterhouse, who on March 16 in that year published an account of it in the *Columbian Centinel*, following it up a few weeks later by showing Jenner's book to the members of the American Academy of Arts and Sciences assembled at Boston.

He did more. Although England was at war with Napoleon at the time, he secured some vaccine from England in the form of infected threads, and on May 8, 1800, used his son Daniel Oliver Waterhouse, then 5 years old, as a subject. As the vaccine pustule reacted on Jennerian lines, he then vaccinated a servant boy. Then, at his request, William Aspinwall, of the smallpox hospital at Brookline, inoculated one of the boys to test the theory that the subject would now be immune from the general disease. And so the boy was. For, though his arms became infected, nothing else was manifest, and Waterhouse could justifiably write, "One fact, in such cases, is worth a thousand arguments," and within six weeks his report, *A Prospect of Exterminating the Small Pox*, was published.

Success was so dramatic and so sudden that it temporarily eclipsed the discovery. For the quacks and charlatans, who are ever on the watch to exploit such things, leapt to administer vaccine. And since their cowpox matter was often impure, sometimes being even mixed with smallpox, yet another epidemic occurred in Boston and a number of people died. Waterhouse then had to endure much the same kind of abuse meted out to early inoculators, and in the end asked the Boston Board of Health to make an investigation. This was duly carried out by a committee of seven practitioners (of whom Waterhouse was one) on 19 subjects, and served to vindicate him completely. Waterhouse followed this up by publishing a second part to his original report, which included letters from Jenner himself, Benjamin Rush, and the President of the United States, who had had his family vaccinated at Monticello in 1801.

From now on Waterhouse continued to stress the importance of inoculating with pure vaccine virus, not with that taken from the vaccine virus after the efflorescence had formed around the pustule. But the effort impoverished him. Professional jealousies and academic intrigues wore him down so much that he resigned his chair when he was only 56 years old. He was able to support his family only by the gift of the medical superintendency of nine New England medical posts, a gift made to him by President Madison. He also campaigned with some success against the use of tobacco, and his *Cautions to Young Persons Concerning Health*, embodying his doctrines, ran to six editions and several translations from its first delivery in 1804. He died, aged 92, in 1846, and lives on in history as the Jenner of America.

W. H. G. ARMYTAGE.

Reports of Societies

RELATION OF FAMILY AND CONSULTANT SERVICES

A meeting of the Sections of Medicine and General Practice of the Royal Society of Medicine on February 23, under the chairmanship of Sir Henry Cohen, devoted itself to a discussion on the relation of family and consultant services.

Changing Relations

Dr. GEOFFREY BARBER, who opened from the point of view of the general practitioner, referred to the changes in relationship between general practitioners and consultants which had taken place during his own experience of practice since 1930. In his early days when he encountered, for example, an acute appendix, he would ring up a fellow practitioner who did surgery and if necessary an operation would be arranged at which he himself gave the anaesthetic. That co-operation was of enormous advantage to the young practitioner because "his bluff was called every time. He knew when he had made an incorrect diagnosis and how he came to make it, and repartees cracked like small-arms fire." That had all been changed. The surgeons who were also general practitioners had largely disappeared. The distance between the general practitioner and the consultant had widened. There were those who appeared to think that the work of the general practitioner must be increasingly to direct his patient to the proper department in which his ailment could be treated. But many still felt that human illness was an intangible affair, and that the general practitioner, with his knowledge of the patient and of his mentality and background, should initiate the medical sequence of events and only when he came up against his own limitations should shepherd his patient to the consultant.

He had found to his horror that he did not always know the consultant to whom he was sending his patient. Unless the personality of the consultant was known one could not confidently choose the right one. Two equally good men, each proficient in his specialty, might be poles apart in their personality. A proper consultation, in his view, was one in which the patient, in his absence, was first discussed between the practitioner and consultant, afterwards in the presence of the patient his case was discussed by them together, and again was discussed between themselves after

the patient had retired. In that way he had continued his own postgraduate education. One form of self-discipline to which he had subjected himself was to put himself in the consultant's place in dealing with some poor old chronic patient who had borne a label for perhaps 15 years, to look at the patient again with the consultant's eye as if he saw him for the first time, and it was astonishing how often one could detect something fresh to modify the label and to suggest something new in treatment.

To narrow the gulf between the general practitioner and the consultant he suggested that general practitioners should follow their cases into hospital, maintaining continuing responsibility for them. From the personal point of view there was a pathetic pride and gratitude in a patient when his general practitioner walked into the ward and he could say to his fellow patients, "This is my doctor." Secondly, the general practitioner must have sufficient pathological and *x*-ray facilities to take the patient up to a certain stage before he sent him to the consultant. Thirdly, he must regard the consultant as his friend and provide him with all the essential information which he had obtained by virtue of being the family doctor.

The Right Use of Hospital Beds

Dr. E. BULMER, who spoke for the consultants, asked that the problem be looked at from the point of view of the right use of hospital beds. The consultant nowadays was always on the hospital staff; formerly many respected family doctors were consultants; those days were gone. Mistakes were often made in hospital in keeping interesting patients for too long; in not admitting early enough that a case was incurable; in admitting patients only for them to die. He viewed with extreme alarm the competition for priorities for hospital beds. Why should cancer always have priority, second only to acute surgical emergency? Could not special hospitals be built for the surgical treatment of the humdrum—piles, hernias, prolapse, tonsils, etc.—and so avoid such competition? In the General Hospital, Birmingham, the number of beds in the medical department was 322, and the number of patients waiting 375, or 1.1 waiting patients for each bed. In the surgical department there were 5.7 waiting patients for each bed. A duty was placed upon the consultant to use his beds properly. Hospitals were too often regarded as dumping grounds for nuisances. The question whether the hospital was the right place for the patient to go to was seldom considered as it should be. No one yet had the courage to say what type of patient should be admitted to hospital, and it was very difficult to deal with situations in which the patient's medical condition was not suitable for in-patient treatment and yet socially admission was imperative. Many forms of illness could be dealt with by the family doctor, with interest to himself and benefit to his patients.

Dr. Bulmer gave a restricted list of conditions which demanded admission on medical grounds. After mentioning that some patients were admitted to hospital for rest and care, he said that care in the modern hospital was certainly excellent, but rest was apt to be non-existent. The decrease in the size of families, the employment of women in industry, and the lamentable ignorance of most young women of the elementary principles of home nursing made it seem to many that the only place to be ill in was the hospital. To-day almost everyone was born in hospital, or their parents would like them to be, and there seemed to be a demand that everyone should die there also. He thought that people should die in their beds at home if that was socially possible.

There should be hand-picking of patients for admission to hospital, Dr. Bulmer continued, but hand-picking was possible only by consultation. The teaching hospitals were in a unique position. In his own hospital about 85% of the patients were hand-picked; the remaining 15% came in through the bed-bureau or by order of the regional hospital board or in some other way.

How popular was consultation? It was popular with part-time consultants, but less so with full-time, who had routine work to do. How popular it was with the family doctor he had no means of knowing. For his own part he wished to see the general practitioner visit his patient in hospital. He was now notifying every doctor when his patient was admitted and had offered him a welcome. This scheme was to be run for a year, and it remained to be seen what the response would be. Ward rounds with general practitioners were growing in popularity. Sunday morning was perhaps the least inconvenient time for the purpose.

The Patient Speaks

Miss ROSE HEILBRON, Q.C. (the first woman to take silk and herself the wife of a doctor), said that after listening to the discussion so far she thought that the only person who had come really well out of it was the patient. Much was heard about the convenience of the doctor, but illness did not always fit into the schedule. The need to call a doctor sometimes occurred on a Sunday or even on Christmas Day. As the mother of a young child she had suffered from the frustration of wanting to call a doctor at some inconvenient hour and being told that she had better wait. The child had a temperature at night and so she called up the doctor at 11 p.m. and braved his wrath. She was not to know that by the next morning the child would be laughing in the doctor's face. She also criticized doctors for not explaining sufficiently to the patient and his family what was wrong. With broadcasting and television and newspapers even the most ignorant lay people nowadays had a little knowledge of medicine and could be entrusted with more explanation. Some health education would also lessen the queues in the waiting-room.

In further discussion Dr. L. W. BATTEN said that he agreed that the home and not the hospital was a good place to be ill in so long as the illness could be managed there, and he rather thought that when he came to die he would like to die at home if possible. Many patients who went into hospital now would be better off at home. But there was a corollary to this, that if the family doctor was to deal with many more types of illness he must have a greatly increased nursing service at his command.

Hospital Beds for the General Practitioner

Dr. H. GUY DAIN spoke of his experience in the war of 1914–18 when he was placed in charge of a Territorial General Hospital to which convoys of sick and wounded were brought straight from the front, and he was responsible for saying what should be done with them. He had behind him surgical specialists and any material aid he required. That was the ideal practice of medicine. The general practitioner should have hospital beds under his control, with the facilities of modern medicine, so that he could be responsible for patients right through their stay in hospital.

Sir HENRY COHEN said that in the discussion a speaker had observed that one of the openers had been looking back and the other forward, but he would remind them of Sir Winston Churchill's comment on history: "The farther back you look the farther forward can you see."

Figures for bed-occupancy unless related to the special circumstances—for example, the type of case, use for teaching or research, or for prolonged observation—could be misleading. In his own wards, three years ago, he had found that patients referred from other consultants had, over a period, a stay on an average of 12 to 13 days, but he would refrain from drawing any specific inference from that fact. It must never be forgotten that the research worker rightly isolated one facet of a problem and studied it intensively. Consequently, he was able to make major contributions to the prevention and control of disease. But the patient, in and out of hospital, was greater than the sum of these scientific isolates and must be studied as a whole personality.

Finally, Sir Henry doubted the validity of economic advantage as the sole criterion of the hospitals' contribution to human welfare. There were imponderables in human happiness and pleasure which, in his view, were of at least equal value.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

The Place of Forceps in Present-day Obstetrics

SIR,—I expected my article on the above subject (*Journal*, October 31, 1953, p. 951) to arouse criticism if only because it was prepared deliberately to provoke discussion at the Cardiff meeting of the Section of Obstetrics and Gynaecology of the British Medical Association. I was therefore surprised and more than a little gratified to find that what I had thought might be viewed as heresy met with such a large measure of approval, not only at the meeting itself and amongst contributors to your correspondence columns, but also amongst a large number of general practitioners and obstetricians in this and other countries who have written or spoken to me privately.

Dr. M. W. Fordham (*Journal*, November 21, 1953, p. 1159) and Dr. A. H. Morley (*Journal*, December 12, 1953, p. 1324, and February 13, 1954, p. 396) appear to be your only correspondents who have been provoked to what could be regarded as adverse comment, although the technical points which they raise impress me as being reasonable and deserving attention if not acceptance. When attempting to cover a large subject within a strictly limited number of words it is difficult to avoid a semblance of dogmatism, but I am sorry that Dr. Morley should have gained the impression that I was writing "majestically"; for humility is essential to good midwifery and any attempt to dictate technique to others is a sign of ignorance.

In regard to axis traction forceps, I only stated that they had been discarded in the hospital whose results I was reporting and that I regarded this development as merely one of many factors contributing to the improvement in these results. It was not suggested that all who practise obstetrics should immediately abandon axis traction forceps; on the contrary, anyone who is trained and experienced in the use of this or any other particular instrument should adhere to it unless he is convinced that a change would improve his results. The pattern of forceps does not matter so much as the judgment and skill of the obstetrician; the good workman can adapt a well-tried and trusted tool or method to meet all manner of circumstances.

Unswerving lifelong loyalty of apprentices to their master, admirable though it may be, can, however, hinder progress, and in this case it ought not to prevent us from recognizing that with the recent rapid evolution of obstetric technique, and from the standpoint of rising generations of obstetricians, the place of forceps having axis traction handles is becoming historical rather than utilitarian. They were introduced for delivery of the head from a high station in the pelvis, and at a time when the mechanism of labour was generally misunderstood. In designing and using them the older obstetricians often sacrificed an accurate cephalic application, or rotated a head from a normal to an abnormal position, in the interests of a pull in the right direction. If it be accepted that caesarean section is now generally preferable to difficult mid-forceps delivery, and that forceps should not be applied (at least in domiciliary practice) until the foetal head has already passed along the greater part of the birth canal, the need is not for an axis traction mechanism but for a simple pattern of forceps which makes for easy observance of the more important principle of an accurate cephalic application. Although axis traction instruments can readily be used on the head arrested at the pelvic outlet, they have no advantage in such a situation. Their potential dangers are that they lure the less experienced operator to reach for a head which is too high to be extracted safely, and they put emphasis on a factor which in these days is not the most important.

Dr. Morley is correct in assuming that the lithotomy position was used in the majority of the forceps deliveries reported in my article, including those in which the mother died from inhalation asphyxia. Space does not permit discussion of the various reasons why the lithotomy position is preferred by nearly all obstetricians throughout the world, but Dr. Morley will find them stated in detail in books such as *Operative Obstetrics* by J. Munro Kerr and J. Chassar Moir.[1] His rather naive explanation that it is because gynaecologists have invaded the realm of obstetrics cannot be accepted, if only because the lithotomy position was widely adopted long before there were any gynaecologists, and some of its strongest advocates to-day are specialists in obstetrics alone. Even if Dr. Morley's suggestion were correct, however, it remains to be asked why the gynaecologist prefers the patient in the lithotomy position for operating.

Nevertheless, it must be recognized that the left lateral position has some advantages, at least in certain circumstances, and that the lithotomy position may have some disadvantages, among which Dr. Morley very properly emphasizes that, according to the type of anaesthesia employed, it may increase the risk of inhalation asphyxia. Here again it is unreasonable to lay down hard and fast rules, and, even if it is generally accepted that the advantages of the lithotomy position ordinarily far outweigh its disadvantages, it does not mean that every obstetrician must use it or that any obstetrician should use it in every case.

Just as Dr. Morley was taught to use axis traction forceps with the patient lying on her left side and has found the method to his liking, I was, soon after qualifying, advised to avoid engaging in public correspondence as far as possible. This explains why I did not reply to Dr. Morley's letters of June 4, 1950 (p. 1319), and December, 1953, letters in which he made his points well and which could safely be left to rest on their own merits. I reply now only because to leave a third letter unanswered might appear discourteous, and because I should like him and Dr. Fordham, as well as other contributors to this discussion, to know that I appreciate their observations, which have helped to fill in some of the many gaps in the original paper. We can certainly ill afford to neglect any suggestion which might reduce the present risks of general anaesthesia in midwifery.—I am, etc.,

Liverpool. T. N. A. JEFFCOATE.

REFERENCE

1 *Operative Obstetrics*, 1949, London.

Rh Antibodies and Domiciliary Midwifery

SIR,—I am sure all general-practitioner obstetricians will be grateful to Dr. M. Chalk (*Journal*, February 20, p. 457) for bringing the subject of Rh antibodies and domiciliary midwifery up for discussion. All who practise domiciliary midwifery are familiar with this problem and will admire the soundness of Dr. Chalk's methods in dealing with these cases, but how many are fortunate enough to have a laboratory with 24-hour facilities close at hand?

First, I would like to underline the need for reassurance to the Rh-negative mothers, most of whom have exaggerated ideas on the gravity of the condition. In this connexion, as well as a precaution should need for transfusions arise later, it is wise to determine the paternal blood group—and a certain number of patients can have their minds put at rest immediately. In the case of a primigravida without a history of miscarriages in whom antibodies are found at the thirty-second week, domiciliary confinement can be permitted, for the risks of an affected baby, let alone a severely affected baby, are negligible. A sample of blood is sent for a Coombs test as a routine. In a subsequent pregnancy arrangements should be made for admission to hospital.

The case of the multigravida is somewhat different, and if antibodies are present she should certainly be confined in hospital. Anybody who has seen an affected baby turn yellow within a few seconds of cutting the cord will surely agree. Even the best-equipped hospital likes to have some notice that a replacement transfusion may be required. It takes some time to mobilize the equipment, paediatrician, and haematologist, and to obtain the correct blood, cross-match and alter the P.C.V., etc. There are no reliable tests to determine in utero if the foetus is affected (the presence of antibodies puts us on guard). Until there are, let us general practitioners, who have a lot of other problems, leave this one to those whose intimate concern it is, for they need all the research material they can obtain.

Unlike your correspondent, I am only too willing to receive instruction on such a complicated and important matter.—I am, etc.,

Southwold. R. H. REYNOLDS.

SIR,—Dr. M. Chalk (*Journal*, February 20, p. 457) raises an important problem. I have notes of over 600 confinements from 1945. Three patients were Rh-negative with antibodies with following results in four confinements. All the children were affected with erythroblastosis.

(1) Mrs. X, 3rd para, confined in hospital. Child was transfused and died after a few hours from cerebral haemorrhage. (2) Mrs. Y, 2nd para, confined in private nursing home. Child alive, not anaemic (Hb 13.6 g.), required transfusion 230 ml. at 3/52. Alive and well. (3) Mrs. Z, 2nd para, confined in private nursing home. Child (cord blood, Hb 9.1 g.) given replacement transfusion immediately after birth in hospital, returned to mother in home the same evening alive and well. (4) Mrs. Z, 3rd para, confined in hospital January, 1952. Stillborn.

I am satisfied that with the help of the paediatrician and the haematologist there was no more delay in case No. 3 than would have occurred in hospital. I am convinced that this help must be laid on for all women with antibodies. In this small series the hospital results were poor, although no blame could be attached to anyone for the result in case No. 4, as the foetus was dead before labour started. I believe that case No. 1 would have had an easier labour at home, as I should not have allowed her to struggle so long with an occipito-posterior without rotating manually. The nursing homes concerned were no better equipped than a decent house.

I conclude, therefore, that these women may be confined at home provided: (1) the home is of reasonable standard; (2) the mother really wants to be delivered at home; (3) the general practitioner is willing to take precautions and enlist the help of the paediatrician and haematologist. I agree with Dr. Chalk that pregnant women should be surrounded with all modern care and attention, but this care should not be so blatant, not to say strident, as is found in many hospitals. The women just get worried to death.—I am, etc.,

Cambridge. C. W. WALKER.

SIR,—As a general practitioner, I agree wholeheartedly with Dr. M. Chalk (*Journal*, February 20, p. 457) that domiciliary midwifery provides distinct advantages over hospital midwifery. If, however, one concedes that 45% of Rh-negative women with antibodies bear affected children,[1] and that exchange transfusion undertaken within the first nine hours of life has been found to be the best remedy for preventing the development of kernicterus,[2] then, I submit, there are grave disadvantages in their delivery at home.

First, the general practitioner *must* be at the delivery to obtain umbilical cord blood for a Coombs test, to do a haemoglobin estimation, and to make a detailed physical examination of the neonate for signs of haemolytic disease. All general practitioners know what such an implacable "must" implies. Secondly, a reassuring negative Coombs may be unobtainable within nine hours of birth. Many laboratories do close at night. Thirdly, hospitals may be loth to take in a neonate for blood tests and observation only, and rightly so, for a case from outside is for them technically not clean. On the other hand, to put a clean baby in a nursery in which it might possibly become infected is hardly fair. Breast troubles in the mother and feeding difficulties in the baby on its return home may be increased.

After one experience of having to leave a busy evening surgery to attend the confinement of a Rh-negative woman with strong antibodies, who refused categorically to enter hospital, of finding that pre-natal arrangements for hospital admission of the suspect neonate had come unstuck, and of finally getting its admission to hospital after three further refusals from other hospitals, I am, for myself, quite certain where Rh-negative women with antibodies ought to be confined.—I am, etc.,

Manchester. ERNEST S. WYDER.

REFERENCES

1 Gaisford, W. F., and Lightwood, R. C. (1953). *Paediatrics for the Practitioner*, vol. 1, p. 87, Butterworth, London.
2 —— (1953). Ibid., vol. 1, p. 90.

Papilloedema in Emphysema

SIR,—I was interested in the very instructive article by Dr. T. Simpson on acute respiratory infections in emphysema (*Journal*, February 6, p. 297). I have examined the fundi of a considerable number of cases of emphysema with severe cyanosis and the findings are quite characteristic. In gross cases the veins are enormously dilated and the tortuous, black sausage-like appearance is very striking. The arteries are often quite normal, although they usually share in the tortuosity. I feel, however, that a word of caution is necessary in interpreting the appearance of the disk as a true papilloedema. It is the rule rather than the exception that the margin of the disk appears to be indistinct in these severe cases, but I think that marked swelling is very uncommon. It would seem that this appearance is due to the dilated veins displacing the tissues of the disk and obliterating the physiological cup, but there is often little or no forward displacement, and when one tries to measure the swelling this is found to be impossible. No case of optic atrophy has been reported, although, of course, papilloedema can subside without this occurring.

I have no doubt that true papilloedema can occur, as Drs. Westlake and Kaye (p. 302) have shown that the C.S.F. pressure can be raised in certain cases and quote an example in which actual retinal haemorrhages were seen with papilloedema, but this type of case must be very rare. In his article Dr. Simpson is aware of the difficulty of interpretation of the disk findings and has only included a few cases in the large number of acute emphysema cases in which he has been certain of the swelling of the disk.

I mention the above points to avoid the diagnosis of papilloedema in cases of emphysema more often than it is actually present.—I am, etc.,

London, W.1. J. GIBSON MOORE.

Medical Needs in the Gold Coast

SIR,—The letter from "Senior Registrar" (*Journal*, February 27, p. 519) raises important questions for all men and women contemplating service in the overseas territories with which the Colonial Office is concerned, and perhaps I may be permitted to offer some comments on the points which he mentions in view of the connexions which I have had with the Colonial Service.

On the issue of a career overseas, it must be admitted that, in the past, officers could look forward without apprehension to a life's work and, on its conclusion, to a pension. While that may not seem so to-day in those territories which are rapidly approaching self-governing status, we must not overlook, for example, the declared statement of the Prime Minister of the Gold Coast that a fully self-governing Gold Coast would need and want the services of overseas officers and that their interests would be fully safeguarded. Is it realistic to expect that any employer of labour could say more than this without inviting a sense of overstatement in the minds of the readers of that statement?

In considering what alternative employment would be open to officers who were no longer required by a territory on attaining self-government, it can reasonably be assumed that in the negotiations leading up to the grant of self-government the question of compensation for loss of career would be one of the important issues to be settled at that date. In 1930, when constitutional changes were agreed upon for Ceylon, officers were given the right to leave the service with compensation for loss of career, and when Ceylon became independent in 1948 an agreement was signed between the Ceylon and United Kingdom Governments guaranteeing the pensions and salaries of existing and retired public servants. When the mandate for Palestine was given up, arrangements for compensation were made. For those officers who would wish to continue in service overseas, every effort would be made to find suitable employment for them, and it should be noted that all medical officers serving in Palestine who wished to continue in service overseas were allocated to suitable posts in the Colonial Service.

While a guarantee clearly cannot be given in advance that it will be possible to follow some precise course on a particular occasion, it is certain that, taking the overseas territories as a whole, British officers will be needed for many years to come and no keen and efficient officer should be apprehensive about his chances of continuing in employment.

Colonial pensions are not paid by the United Kingdom Government, since that Government is not the employer of officers in the Colonial Service. The payment of pensions is a liability of the Colonial Government which employs the officer. As was mentioned above in connexion with compensation for loss of career, the negotiations leading up to the grant of self-governing status would also cover the payment of pensions. There is no evidence, so far, to suggest that this aspect also would not be settled satisfactorily or that the terms of settlement would not be honoured. Your correspondent asks whether there is any guarantee that pensions would continue to be paid. One can only answer this by asking another question: What evidence of any default is there, so far, which would justify apprehension on this score?

I hope that your correspondent and others who will read this letter will appreciate that there are really no grounds for apprehension, either about the payment of reasonable compensation if careers are cut short, or about the payment of pensions when an overseas territory achieves self-government. Where this has happened to date, satisfactory arrangements have been made and there is no reason to suppose that the same will not be the case in the future.—I am, etc.,

Cardiff. FREDERICK HEAF.

Lumbar Puncture

SIR,—It is unfortunate that Dr. J. N. Cumings in his article on "The Cerebrospinal Fluid in Diagnosis" (*Journal*, February 20, p. 449) should advocate anew the procedure of lumbar puncture in cases of intracranial and spinal tumour. The majority of the younger generation of neurologists and general physicians are alive to the danger of this investigation producing tentorial or medullary pressure cones and realize that very little information of value accrues from its use. This enlightened view was well put forward by Dr. W. Goddy in your issue of November 7, 1953 (p. 1040). Once the suspicion of space-occupying lesion within the skull has arisen upon clinical grounds the appropriate investigations are those of radiography of the skull, air study of the ventricular system and/or angiography, the aim being to localize the expanding lesion in order to give the neurosurgeon the best chance of making a radical cure, if this be possible.

Lumbar puncture disturbs the pressure relationships within the skull and spine, frequently produces an ingravescence of symptoms or signs and occasionally death within 24 to 48 hours as a result of slow seepage of cerebrospinal fluid into the extradural spinal tissues, with the precipitation of a medullary or tentorial pressure cone. Once this vicious circle has been established the chances of a successful result from surgery are gravely prejudiced. Lumbar puncture is dangerous enough, but the added insult of jugular compression is the one measure calculated to initiate pressure coning at the tentorium or foramen magnum. Similarly, lumbar puncture in cases of spinal compression is highly dangerous and often the cause of sudden onset of bladder and bowel complications or of rapid worsening of the clinical picture. When necessary to aid in the diagnosis of spinal tumour, lumbar puncture should be performed on the same day as, and as a preliminary to, myelography and laminectomy in an attempt to relieve the compression.

Lumbar puncture has a use when properly employed in suspected cases of spinal tumour, but it has no place, or value, in the investigation of patients suffering from suspected intracranial tumour.—I am, etc.,

London, W.C.1. WYLIE MCKISSOCK.

Sterilization of Ampoules

SIR,—It is evident that I owe an apology to Dr. D. Reckless (*Journal*, February 20, p. 455) for the ambiguity in my letter (*Journal*, February 6, p. 355). Lignocaine ("xylocaine"), which I use for practically every extradural block that I do, is supplied in ampoules (or possibly they are better described as phials) made of thick glass and closed by a small rubber plug. This latter can be removed without the slightest risk of any glass being broken. Bacteriological examination of the ampoules' contents has never shown contamination having occurred through the thick glass. So I can assure Dr. Reckless that the technique is absolutely safe, and I am sorry that the lack of clarity in my letter should have happened.

Concerning his admonition to examine the contents of ampoules prior to intrathecal injection, this is advice I am unable to take for the simple reason that I abandoned spinals in favour of the very satisfactory and, I suggest, safer extradural block, six years ago. There is an abundance of good advice in the literature on how to find the extradural space: if Dr. Reckless is still content to encounter the "only disaster" of a fruitless entry into the theca, then I suggest that these are the words of wisdom that have fallen on stony ground.—I am, etc.,

London, S.W.15. G. C. STEEL.

Reaction to Blood Transfusion

SIR,—I suggest that the fears expressed by Dr. R. D. Barnard (*Journal*, February 6, p. 332) are unjustified because he does not take into account the indications which serve to show when dextran is likely to benefit the patient. The principal indication for dextran is oligaemic shock due to haemorrhage, whether evident or concealed as in crush injuries, or in concealed accidental haemorrhage of pregnancy; and the purpose of its administration is to increase blood volume so that the circulation again becomes effective. Dextran is, in fact, a plasma volume expander and we use it as such, either alone or as a stop-gap, until properly grouped and cross-matched blood can be obtained. We have administered about 1,300 bottles to about 600 patients, and encountered only one reaction sufficiently severe to warrant our stopping the infusion. We do not often administer more than 1,000 ml. 6% dextran to one patient, but we have given 1,500–2,000 ml. occasionally without any serious reactions; all these infusions have been given to patients with haemorrhage or crush injury, and a few have saved lives.

If dextran is used in this way its "conglutinin" powers do not matter. Even were it to increase anti-A or anti-D titres a thousandfold, the patient would not suffer provided that ABO and D homologous blood were administered. In England to-day few transfusionists consider group O blood to be "universal donor" blood, and even in America I believe it is usual to add Witebsky's group-specific substances to neutralize the agglutinins of group O blood which is to be used as "universal donor" blood. Anyone knowing of the "conglutinative" powers of dextran would expect that if a sufficient quantity of dextran were administered to patients whose blood contained high titres of auto-antibodies an episode of acute intravascular haemolysis would follow. Fortunately, auto-antibodies are fairly uncommon except in acquired haemolytic anaemia, atypical pneumonia, and leukaemia, and are rare in neoplastic disease. It is very unusual for patients with these diseases to require treatment with a plasma volume expander, and I am a little surprised that Dr. Barnard has been able to obtain experimental confirmation that dextran given to such patients causes haemagglutination and (presumably) haemolysis.

In the patient with severe oligaemic shock, treatment must be directed to restoring blood volume. In many patients the *vis medicatrix naturae*, with warmth and fluids by mouth, will suffice; others can tolerate a few hours' delay while blood is obtained; but there remain some who need blood volume restoration as soon as possible. In this last group one must choose between plasma—which carries a 1% risk of hepatitis—and dextran, the dangers of which appear to be theoretical

—unless, of course, one is to fly to the blood bank and demand blood at once, thus increasing the risk of incompatibility. Dr. Barnard's fears seem to be based mainly on work *in vitro*. I agree that when dextran is mixed with blood in the test-tube many peculiar things happen: but if dextran is mixed with the blood remaining in an exsanguinated patient the patient gets better.

I have never done "dextran compatibility tests" and I do not intend to start until it is shown that they would serve a useful purpose; nor do I propose to allow Dr. Barnard's largely theoretical fears to overwhelm my practical experience, which is that patients who have had a sudden severe haemorrhage can usually be revived by dextran infusion, and that in such circumstances dextran is safer than plasma or whole blood.—I am, etc.,

London, N.W.10. GEORGE DISCOMBE.

"Status Lymphaticus"

SIR,—In his article on "Status Lymphaticus" (*Journal*, January 16, p. 149) Dr. H. B. Dodwell, presumably in support of his views, quotes from Boyd's *Textbook of Pathology*[1] the author's statement that "there is no proof that the thymus gland has anything to do with stoppage of the heart." A few lines above this Boyd writes: "There is no doubt that the diagnosis of status lymphaticus or enlarged thymus has been much misused at coroners' inquests, but on the other hand there does appear to be some relationship between lowered constitutional resistance to certain otherwise trivial injuries and a condition of lymphatic hyperplasia. I may quote the following case from the medico-legal practice of my colleague Dr. Erb, which is surely sufficient proof that the concept of death from status lymphaticus is not a pure myth. One of a group of children who were playing on the road was struck down by a motor car and injured. He did not die, but a little lad watching the accident from an adjoining lawn fell dead. At post mortem the child was found to have an enlarged thymus, a thin-walled hypoplastic aorta, and marked hyperplasia of the lymphoid tissue throughout the body."

I submit that if the above illustrates the way in which Dr. Dodwell has made use of the subject-matter reviewed then his researches on the subject of status lymphaticus, which appear to be entirely literary, must be regarded with misgiving.—I am, etc.,

Alloa. W. B. LAING.

REFERENCE

[1] *Textbook of Pathology*, 1947, 5th ed., London.

SIR,—May I reply to the letters criticizing my article on the above subject (*Journal*, January 16, p. 149) which have appeared in the *Journal*? Dr. H. Ucko (*Journal*, February 13, p. 398) would appear to be discussing an entirely different pathological condition; no report of any case of status lymphaticus that I have ever read has described a patient who, prior to unexpected sudden death, displayed anatomical anomalies, recurrent asthma, lymphocytosis, and evidence of the breaking down of the nuclei of lymphocytes. Had this syndrome been associated in this country with sudden death surely a few cases among the two hundred odd deaths per annum would have been described.

Dr. C. Langton Hewer (*Journal*, January 30, p. 274) raises two points of objection to my views—the late Sir Bernard Spilsbury's expressed opinions, and my denial of Dr. Kemp's case records. With regard to Sir Bernard's view, there is no supporting published evidence, the Medical Research Council's Committee found no association between enlarged thymus glands and enlarged lymphatic glands, the only writers to publish a series of narrowed aortae in unexpected deaths found no enlargement of the thymus gland, and I have failed to find any collection of cases of fatty infiltration of the myocardium in sudden death in the young. As to Dr. Hewer's view that it is incredible that Sir Bernard could have pursued a chimera for so many years, surely it is equally incredible that the twelve distinguished members of the Medical Research Council's Committee should have been thoroughly misled after such painstaking collecting and weighing of evidence?

Turning to Dr. Hewer's second point, I certainly owe Dr. Kemp an apology for stating that he did not cite any cases; he did not do so in the article originally quoted by Dr. Hewer but did cite five cases in his article (which I overlooked) in the *Canadian Medical Association Journal* for 1933 and which, together with two other cases, were reported again in *Elementary Anaesthesia*.[1] I cannot agree with Dr. Hewer in regarding this article as an excellent account, since only a bare majority of the cases have the weights of the thymus glands recorded and all the deaths are capable of another explanation—thus, of the two tonsillectomies, that with the really large thymus gland was found after death to have some blood in the lower trachea, and that with the slightly enlarged thymus some venous congestion of the lungs. Of the five non-operative cases, in only two is the weight of the thymus gland stated; both infants found dead showed cardiac petechiae and the other three cases had been ill for from fifteen hours to two days, one of them having a "chest full of rales" shortly before death.

Finally, in his historical account of status lymphaticus Dr. Kemp, in dealing with the article published in Vienna in 1889 from which Osler took his account,[2] states that Dr. Paltauf had "access to a vast quantity of clinical pathological material and from his wide experience advanced the view . . ."; Dr. Kemp is obviously confusing the author with his elder brother, since the author Arnold Paltauf died in his thirty-third year, four years after the article was published, while it was his elder brother Richard Paltauf who subsequently became in 1898 professor of pathology in Vienna, dying in 1924.—I am, etc.,

London, N.7. H. B. DODWELL.

REFERENCES

[1] *Elementary Anaesthesia*, 1948. Baillière, Tindall and Cox. London.
[2] *Principles and Practice of Medicine*, 1898. 3rd ed. London.

SIR,—The cycles of the old, and some of the new, arguments for and against "status lymphaticus" have been moving again in your correspondence. The observations of Dr. H. Ucko (*Journal*, February 13, p. 398) are not only interesting but seem to relate reasonably thymic hyperplasia with adrenal, or pituitary adrenocortical, deficiency in a lack of resistance to stress.

In gross morbid anatomical study of cases of "status lymphaticus" 25 years ago I noticed that a common finding was peculiarly small adrenals. I am now therefore quite interested in Dr. Ucko's final observation that the hypothesis (adrenocortical deficiency) could easily be verified by investigations into the adrenal cortical reserve of cases with suspected status thymo-lymphaticus. Perhaps some specially skilled team will take up this well-worth-while study.—I am, etc.,

Bristol. A. V. NEALE.

Cortisone and Manipulation of Knee-joint

SIR,—With all due deference to the distinguished members of the Medical Research Council subcommittee, I would like to make a few comments on their recent report (*Journal*, January 30, p. 233) concerning the effect of cortisone as an adjuvant to manipulation in rheumatoid arthritis. No one to-day would use systemic cortisone in preference to topical hydrocortisone to cover the manipulation required to straighten a knee-joint fixed in flexion. It is presumed that when these therapeutic trials were initiated hydrocortisone was either not readily available or its advantages in this situation were not recognized; in either event, it would be interesting to observe the result of further studies, similarly controlled, using intra-articular hydrocortisone.

It is noted that in all cases in this series the contralateral knee was also affected, though less severely than the one selected for manipulation; however, there was no significant difference between the cortisone-treated and codeine-treated groups, the contralateral knee in each group showing some slight improvement. To anyone not entirely familiar with the indications for cortisone therapy, these results might

seem surprisingly negative; but it should be recalled that patients with "severe disease activity" were excluded from this study, and it is only in so far as active inflammation exists in a joint that cortisone can be of temporary benefit. Since in these patients deformities had been present for a minimum of six months, it is reasonable to assume, in the absence of any information to the contrary, that in most of them the arthritis had reached the chronic fibrotic stage in which little if any inflammatory reaction persisted.—I am, etc.,

J. H. LAURIE.
Medical Director, Merck & Co., Ltd.
Montreal.

Whither Anaesthesia?

SIR,—The letter of Dr. Charles E. Sykes (*Journal*, February 6, p. 336) expresses the view of most anaesthetists. The race to be first with the news could be laughable were it not so dangerous, because false facts often endure for a long time. The confidence and comparative ease with which barbiturates and relaxants were so successfully introduced into anaesthesia became presumptuous in the case of hypotension and the bloodless field, even though the dangers were obvious. Doubtless the very highly skilled escaped disaster or confined its use to those cases where the risk is justified, but others were either not so skilled or so lucky. It should be a sobering thought that the majority of these misfortunes could have been avoided if well-established methods had been employed, since, if there is sufficient skill and experience available, the patient unfit for anaesthesia scarcely exists to-day. There was some lack of discernment in the conclusions of many of the research workers in this field.

Our profession very properly defends and encourages the right of freedom of action among its members. It holds, however, that this right implies a responsibility, and the opportunity an obligation. The introduction of every new anaesthetic agent results in a flood of reports of strange reactions, most of which fortunately appear to happen only to a few, and which, after a while, no longer seem to happen at all. Such reports only cause confusion or amusement, since errors of technique and judgment are always possible. Otherwise why are the majority of anaesthetists spared these dramatic experiences when the drugs are in daily use?

Hypothermia is now in the news. Is it too much to ask whether the promised benefits are sufficiently great to justify haste in its use, and if it is not possible that research should be carried out by those with the experience and the facilities to do it adequately? Surely some control is justifiable to ensure that the hypotensive debacle is not repeated, and that our inevitable progress is sane, safe, and satisfactory.—I am, etc.,

G. DONAL MCGRATH
Deal

Controlled Hypothermia

SIR,—Drs. P. R. Mesham and W. E. B. Scott (*Journal*, February 20, p. 455), while discussing the possible site of action of chlorpromazine, state, "We include in our conception of the autonomic system those centres in the hypothalamus and elsewhere which co-ordinate and integrate the functions of this system." Such a wide interpretation of the autonomic nervous system may well justify the claims of the above authors (together with Drs. J. W. Dundee and T. Cecil Gray) in a previous paper entitled "Hypothermia with Autonomic Block in Man,"[1] but it opens the term "autonomic blocking-agent" to include practically every known anaesthetic agent.

No one would question the close association of the hypothalamus with the autonomic system, but are we justified in describing any drug which interrupts the normal mechanism of thermo-regulation as an autonomic blocking-agent? Any anaesthetic drug which produces unconsciousness disrupts the heat-regulating mechanism, and, provided shivering is prevented, the patient's body temperature rapidly approaches that of his environment. Chlorpromazine, therefore, is but one of a multitude of drugs available for lowering the body temperature, and it remains to be proved that it possesses any advantage over routine and established anaesthetic techniques.

Professor G. A. G. Mitchell, in his excellent book *Anatomy of the Autonomic Nervous System*,[2] classifies this system into "a central part which includes centres located in the cerebrum, cerebellum, brain stem, and cord," and "a peripheral part which consists of two paravertebral ganglionated trunks and various prevertebral, visceral and vascular nerve plexuses. . . ." If we are to name any drug that acts on this vast network as an "autonomic blocking-agent," then the confusion will be great.

In the interests of clarity, therefore, may I suggest that we should abandon the term "autonomic blocking-agent" at its birth, and return to the parental term from which it obviously sprang—that is, "autonomic ganglion-blocking drug"—a name which has a specific meaning in both physiology and pharmacology?—I am, etc.,

H. C. CHURCHILL-DAVIDSON.
London, S.E.1.

REFERENCES
[1] *British Medical Journal*, 1953, **2**, 1237.
[2] *Anatomy of the Autonomic Nervous System*, 1953, E. and S. Livingstone.

The Unsaturated Fatty Acids

SIR,—In answer to Dr. Eric Lodge's inquiry (*Journal*, February 13, p. 395), one of my partners and I have had some experience of the unsaturated fatty acids in the treatment of leg ulcers in elderly women. These cases healed up well on the treatment. We also found that if the ulcer is infected with *B. pyocyaneus* the ointment was not successful until the *B. pyocyaneus* was killed off; and we found dibromopropamidine isethionate ("brulidine") the most useful cream for this purpose.

We also tried this treatment in two cases of psoriasis. One healed in the course of three months and has not relapsed as far as we know (18 months). The other did not respond to the treatment until ung. dithranol was applied at night. It is now responding very well.

In conclusion we found this treatment most efficacious in the treatment of bedsores.—I am, etc.,

CHRISTOPHER PETIT.
New Malden, Surrey.

Intravenous Iron

SIR,—I very much enjoyed Dr. J. A. Nissim's article on intravenous iron (*Journal*, February 13, p. 352). I would appreciate the hospitality of your columns to reply to some of the points raised. I entirely agree that the question of iron precipitation is of great, if not fundamental, importance. Although it has been shown to occur in animals, there is as yet no evidence, as Dr. Nissim himself admits, that it occurs in man with *normal dosage*, which means, I think he will agree, a maximum of 100 mg. Fe per injection. I am prepared to admit that the iron moiety may not be involved and that my tuberculous cases[1] were not strictly normal cases of iron-deficiency anaemia. Nevertheless, I do not think that impurities in the saccharated component are fundamental causes of reactions. After all, many thousands of injections must be given annually, and only a small fraction cause reactions severe enough to be talked or written of. Surely one should expect more. Betty Holt[2] has told us that in India reactions are rare despite the fact that the same compounds are used there. Although not strictly apposite, intravenous glucose and glucose saline are given very frequently, but little is heard of painful reactions from this cause. I have no doubt, however, that the compound is locally irritating, for maladministration in my hands has produced some painful and swollen arms from extravenous extravasation. I have tried, without success, to get some saccharated component itself, as I felt that investigation of this moiety would yield interesting information.

It is my experience with the use of antisera, especially anti-diphtheria, that has led me to stress the importance of an altered antigen–antibody reaction in these cases. Landsteiner's[3] classical experiments with *para*-arsanilic acid showed that it was its combination with protein, and not the compound itself, which was important. Combinations of bacterial polysaccharides with protein similarly act as

haptens. Protein is therefore essential in the production of antigenic effects. This does not seem to me to be incompatible with any theory of the cause of these iron reactions, for either the iron or the saccharated components could combine with the subject's protein to act as an antigen. With regard to paroxysmal haemoglobinuria, this is another example of a violent and abnormal antigen–antibody response—namely, an abnormal cold haemolysin. The reticulo-endothelial system activity can therefore be invoked not as a cause but as an effect of this abnormal reaction.

As to the age of the patient, my limited experience of its use in the old was encouraging in that I thought injections were tolerated better or as well as in younger subjects. There were no reactions in my cases. I have had no experience of injections in children, but the fact that reactions are commoner among them and young adults may be linked with their increased susceptibility to abnormal antigen–antibody effects—e.g., asthma, serum sickness, and so on—just as such effects are rarer in the old.—I am, etc.,

Romford, Essex. I. M. LIBRACH.

REFERENCES

1 *British Medical Journal*, 1953, 1, 21.
2 Ibid., 1953, 1, 834.
3 *J. exp. Med.*, 1924, 39, 631.

SIR,—I hope that the possibility of toxic reactions reported in Dr. J. A. Nissim's interesting paper (*Journal*, February 13, p. 352) will not dissuade others from the use of this valuable remedy. We have used saccharated iron oxide, mainly for anaemia in rheumatoid arthritis, for four years, and in the last two years or so have been impressed by the lack of toxic reactions. We have used "neoferrum" throughout this latter period. Complete figures are only available since the beginning of 1953. Since then, 117 patients have been given 899 injections (107 of the patients had rheumatoid arthritis). No serious toxic effects and no venous thrombosis occurred; the only "complications" seen were the following: One nervous girl complained of "tingling fingers and a faint feeling" shortly after the first two injections, lasting about 15 minutes. She completed the course without further upset. Two women, given injections during menstruation, thought their loss was heavier for a day after the injections.

Clinical evidence of visceral arteriosclerosis is an indication for caution and the maximal dose may need to be restricted to 100 mg. I do not now think that age of itself, however, is a contraindication. During the period in question, 14 patients over 65 years of age were treated without any ill effects; the eldest was 79 and was treated as an out-patient.

The following practical points may be worth mentioning. Injections are given thrice weekly as a rule, but sometimes daily, using hypodermic needles (size 12), the injection of 10 ml. taking about one minute. These small needles limit the rate of injection and enable veins on the back of the hand to be used when elbows are fixed in flexion. Total dosage is calculated to raise the haemoglobin to 100% (on the basis that 100 mg. iron raises the Hb by 4%), with 50% of the dose added. The initial dose is usually 50 mg., followed by 100 mg., and then 200 mg. injections to the required amount. In frail patients the first dose may be reduced to 40 mg. or less. Care must of course be taken that the injection is *wholly intravenous*. After injection the arm is raised for a few minutes without any local pressure and the patient rests for a few minutes more (we insist that patients must be recumbent); out-patients are detained for at least 15 minutes.

At least in anaemic cases of rheumatoid arthritis, intravenous iron appears to be a safe remedy, though not, of course, invariably effective.—I am, etc.,

Bath. M. R. JEFFREY.

The Thyroid

SIR,—Dr. I. Doniach (*Journal*, February 27, p. 503) ends his review of my book, *The Thyroid, a Physiological, Pathological, Clinical, and Surgical Study*, with the remark, "But I am afraid that the work as a whole would irritate the serious student beyond measure." The perceptive reader will have gathered from the tone and substance of the review that Dr. Doniach, who is a pathologist, does not agree with the conclusions that I have reached from a study of the material obtained from 2,114 consecutive thyroidectomies. Though we must agree to differ I see no reason why there should be any feeling of irritation on either side: time will show where the truth lies.

In fairness to prospective readers may I be allowed to point out that more than 400 out of the 600 pages of the book deal with the anatomy and physiology of the gland, and with the clinical aspects of thyroid diseases and their medical, radiotherapeutic, and surgical treatment. And as to the pathology of the thyroid, if Dr. Doniach will be good enough to re-read my book more carefully he will find that his queries are fully dealt with.—I am, etc.,

London, W.1. T. LEVITT.

Diagnosis of Thyrotoxicosis

SIR,—I read with great interest Professor E. J. Wayne's paper on the diagnosis of thyrotoxicosis (*Journal*, February 20, p. 411). Some time ago, while following up a number of thyrotoxic patients treated with methythiouracil, I noticed that as they became euthyroid a sinus arrhythmia appeared. It occurred to me that it was perhaps possible that hyperthyroidism with its increased sympathetic tone abolishes sinus arrhythmia, and therefore one could exclude, in most cases, a diagnosis of hyperthyroidism if sinus arrhythmia is found. Once aware of this possibility, I have looked for this sign in a number of cases in which a suspicion of hyperthyroidism was raised by the presence of palpitations, sweating, tachycardia, etc.,

So far I have been satisfied that no cases showing sinus arrhythmia have proved, after further investigation, to have thyrotoxicosis. As I have seen no references to this matter in the literature, I venture to make this observation known, as it may be of help in doubtful cases.—I am, etc.,

London, N.19. E. MONTUSCHI.

SIR,—We feel that the article by Professor E. J. Wayne (*Journal*, February 20, p. 411) and the leading article of the same issue (p. 443) contain certain experimental and bibliographical inaccuracies which deserve comment.

It was Robertson and Reid[1] and not Robertson[2] who "pointed out that a specially careful technique and standards derived from normal persons in Great Britain should be used" for estimation of the B.M.R. Robertson[3] drew attention to the value of the effect of iodine on the B.M.R. as a diagnostic test for thyrotoxicosis, of great value when the thyrotoxicosis is mild and the B.M.R., though raised for the patient, yet may fall within the normal range, and Means[4] stated this a year previously. It is not our experience that B.M.R. "observations on out-patients are often unsatisfactory" or that "the test can be conducted satisfactorily only on the in-patient." To quote from a previous paper by Robertson,[5] "this is an entirely false conception without any experimental evidence to support it." Around 1930 both Benedict and DuBois told one of us (J. D. R.) that B.M.R. tests on ambulatory patients were as accurate and reliable as those carried out at the bedside, if half an hour's rest on a comfortable bed in a warm room at a temperature around 20° C. precedes the determination. Full details are given in the paper just quoted, in which paper Benedict and DuBois's views were amply confirmed.

With regard to the determination of serum protein-bound iodine, the pessimistic note struck by both Professor Wayne and your leader writer is contrary to our experience. One of us (Kirkpatrick[6]) has recently discussed the practical aspects of a method somewhat different in principle to that used by Professor Wayne, and has indicated the precautions needed to avoid the most serious of the difficulties that may arise. We have employed this method routinely in this department during the past two years, and have found it of great assistance in the assessment of thyroid status, the time and cost involved comparing favourably with those of a determination such as the 17-ketosteroids in urine which is now a more or less familiar feature in clinical bio-

chemical work. We feel justified, therefore, in having a more hopeful outlook regarding the extension of availability of the determination to clinicians, especially as stimulation of interest is prerequisite to improvements in accuracy and technique.—We are, etc.,

H. F. W. KIRKPATRICK.
J. DOUGLAS ROBERTSON.

London, W.1.

REFERENCES

1 *Lancet*, 1952, **1**, 940.
2 Ibid., 1952, **1**, 511.
3 Ibid., 1934, **2**, 1076.
4 *Ann. intern. Med.*, 1933, **7**, 439.
5 *British Medical Journal*, 1944, **1**, 617.
6 *Analyst*, 1953, **78**, 348.

College of General Practitioners

SIR,—In answer to Dr. D. G. Berry (*Journal*, February 27, p. 520), we would like to say that the arrangement to send the College's Research Newsletters to members on the Research Register only (before publishing them in the *Practitioner* and subsequently in the Annual Report) is a Council decision which could be changed if the expense of circulating nearly 3,000 members and associates with frequent letters was considered justifiable. During the past year you have kindly published in your *Journal* more than a dozen notices about the activities of the College which many members have seen.

The time for lectures delivered to *undergraduates* last autumn (5.30 p.m.) was deliberately chosen, after discussion with medical schools, as being that most suitable for medical students. Any similar course of lectures for postgraduates will clearly be arranged at times which will not clash with normal surgery hours.

Some regional faculties have already been formed in the provinces and overseas, which, with others now being developed in London and elsewhere, will provide information on all College activities for those members and associates who wish to play an active part.—We are, etc.,

G. F. ABERCROMBIE,
Chairman of Council.
J. H. HUNT,
Honorary Secretary.

College of General Practitioners, London, E.C.4.

The Feeble-minded

SIR,—The paper by Drs. N. O'Connor and J. Tizard (*Journal*, January 2, p. 16) was welcome as a piece of factual information, especially where it depended on the observations over a wide range of hospitals of one team of workers. This kind of knowledge is hard to come by. It is a pity that it made a text for the unhelpful suggestions in the annotation (p. 35) and, apparently, elsewhere to which Dr. J. M. Crawford refers so wisely and so clearly (*Journal*, February 13, p. 395). I endorse his every word, particularly about the treatment of the feeble-minded.

It is true that there is some variation in policy between one hospital and another—we have not reached the dullness of certainty that there is only one best way—but to his statement from Botley's Park I can add one on the practice of the hospital for which, until recently, I had been responsible for 20 years. Each patient was regarded as an individual rather than as a member of a group, and none was "detained for an indefinite period" because he "might become" difficult. The aim was to develop and train each one as far towards life in the community as it seemed possible for him to go. Apart from such psychiatric adjustment as was necessary, the stages were freedom of movement within the hospital, parole in the neighbourhood, short leaves, long leaves, full licence, and possible discharge. At the same time there was social and occupational training within the hospital leading to daily work outside the hospital, usually of progressive responsibility and importance, and then to useful employment on licence in employable cases. The process took only a short time for a few patients, even when admitted with a lurid history; for some it took years and several trials and failures; and for many the full grade could never be made. But the hope and the effort were always there, and the patient's capacity and ability were estimated and his treatment and progress judged—in fact he was fathered and mothered by the team of doctors, nurses, trainers, teachers, and other staff, the social workers and, when possible, the parent or friend outside under the guidance of the psychiatrist.

The fallacy in the annotation, and it was suggested in Tizard and O'Connor's earlier paper[1] on the factory experiment at Darenth, is that employment is the main object and employability the criterion. As Dr. Crawford makes clear, the long aim of all treatment is the wider one of social rehabilitation, to enable the feeble-minded person to live in the community with reasonable success and with comfort to himself and his neighbours.—I am, etc.,

NOEL H. M. BURKE.

Wimbledon, S.W.19.

REFERENCE

1 *Lancet*, 1952, **2**, 620.

Eli Lilly Medical Research Fellowship (South Africa)

SIR,—May I, through the courtesy of your columns, draw the attention of medical practitioners registered in South Africa, who may at present be in the United Kingdom, to the fact that applications may be submitted for the 1954 award of this Fellowship? The value of the Fellowship is $250 a month for 12 months, plus return travelling expenses to the point of study in the United States of America. Further details can be obtained from the undersigned. The closing date for applications is June 15, 1954.—I am, etc.,

H. A. SHAPIRO,
Honorary Chairman, Selection Committee,
Eli Lilly Medical Research Fellowship (South Africa).

Capetown.

A New Oral Diuretic

SIR,—Referring to Dr. Myer Cohen's letter (*Journal*, February 13, p. 394) under the above title, I too found your annotator's arguments regarding "mercloran" unconvincing if not actually misleading, and with no other information than from your annotation would have dismissed the preparation as unreliable as previous oral mercurials. I had, however, used mercloran in a number of cases, both before and after your annotation appeared, both under hospital conditions, with measured fluid intake and output, and also in the home. My technique has, however, been that suggested by the manufacturers—the administration of one tablet, three or four times daily, supplementary injections of a mercurial being given once weekly or less frequently. The results have been entirely satisfactory, the basal output being in most cases greatly increased, with no gastro-intestinal upset, a result I have never achieved with previous oral preparations.

Given as recommended above, mercloran should prove a most valuable aid to the general practitioner, in keeping his cardiac cases oedema free, without unpleasant side-effect.—I am, etc.,

T. N. RUDD.

Tiverton, Devon.

Westminster Abbey Appeal

SIR,—During the course of last year you were good enough to draw the attention of your readers to the Westminster Abbey Appeal Fund. I shall be grateful if you will now allow me through your columns to thank all the members of the medical profession who so kindly responded to the Appeal. It has proved impossible to write to all contributors personally, beyond sending them an official receipt, but I hope that these few words will serve to assure them one and all of the sincere gratitude of the Dean and Chapter of Westminster. There is good hope that before the Fund finally closes down the target of a million pounds will have been reached.—I am, etc.,

ALAN C. DON,
Dean of Westminster.

London, S.W.1.

Obituary

K. H. DIGBY, O.B.E., M.B., F.R.C.S.

We record with regret the death of Professor Kenelm Digby in London on February 23 at the age of 69. For many years he was professor of surgery in the University of Hong Kong, and since his return to England he had been doing surgical research work at the Royal College of Surgeons.

Kenelm Hutchinson Digby, the son of the late William Digby, C.I.E., was born at Ealing on August 4, 1884. From Quernmore School, in Kent, he entered Guy's Hospital Medical School, where he had a distinguished career as a student, winning the Michael Harris, the Hilton, and the Beaney prizes. After graduation in 1907 he held a number of resident posts at Guy's, and was surgical registrar there from 1909 to 1911. Meanwhile he had taken the F.R.C.S., and in 1912 he was appointed principal medical officer of the Great Central Railway. He held this post for only one year, however, for in 1913 began his long association with the Colony of Hong Kong, where he took up the appointment of professor of anatomy in the university which had been opened the previous year. He occupied the chair until 1923, when he became professor of surgery; since 1915 he had also been Ho Tung professor of clinical surgery in the university. He relinquished both surgical chairs in 1945, when he was appointed emeritus professor. From 1915 to 1948 he was honorary consultant in surgery to the Government of Hong Kong and from 1930 to 1948 surgeon at the Queen Mary Hospital in the island. In the Birthday Honours in 1939 he was appointed O.B.E. for his medical services in Hong Kong. Interned in the Stanley Camp by the Japanese during the last war, he returned to this country in 1949 and had since been engaged in research work at the Royal College of Surgeons of England's surgical research farm at Downe, in Kent.

Professor Digby's medical interests were wide, and he turned his inquiring mind to problems both within and outside the scope of clinical surgery. He published many papers on a great variety of subjects and, in 1919, a book entitled *Immunity in Health: the Functions of the Tonsils and the Appendix*. His ingenuity and versatility were remarkable, and he enjoyed devising his own equipment. At the Scientific Exhibition at the Annual Meeting of the B.M.A. in Cardiff last year he demonstrated methods of investigating the functions of the subepithelial lymphatic glands.

A member of the British Medical Association for many years, Professor Digby was president of the Hong Kong and China Branch in 1946, and after his return to England served on the Council of the Association from 1952 until January of this year (when he resigned) as the representative of the Borneo, Ceylon, Hong Kong and China, and Malayan Branches, and on the Overseas Committee during the same period. He married Miss Selina D. Law in 1913, and there were two daughters of the marriage.

We are indebted to Professor L. J. DAVIS for the following appreciation: As a man, Digby was remarkable for his integrity, his honesty of purpose, his enthusiastic attitude to life, and his complete absence of smallmindedness. His colleagues in committee sometimes found him somewhat intransigent when there were differences of opinion, but his opinions were often vindicated by time, and he never nourished rancour. If he did disagree with people he never spoke ill of them. He had no enemies, but many friends among people of all positions and races.

As a teacher, he was remarkable for his zeal, which never flagged notwithstanding advancing age and adverse climatic conditions. Many hundreds of medical students who have passed through his hands owe much to him for his sound teaching of the principles and practice of surgery. As a surgeon he was quite first-rate. He neglected no opportunity of extending his knowledge of new developments, and during his leaves of absence from Hong Kong he visited most of the leading surgical centres in Europe and the U.S.A. Despite his heavy commitments as a teacher and a practitioner of surgery, he took a lively interest in research. He wrote papers himself and stimulated his associates to do likewise. Throughout his life he maintained his interest in the role of lymphatic tissues in immunity. Only just recently he demonstrated an exhibition of this subject before a scientific society in this country. News of his death will be learnt with great sorrow by his former colleagues, patients, and students in the Far East and elsewhere.

F. R. SELBIE, M.D., Ph.D., D.Sc.

Professor F. R. Selbie, professor of bacteriology at the Middlesex Hospital Medical School since 1949, died suddenly in London on February 22 at the age of 49.

Frederick Robert Selbie early gave evidence that he was destined for high academic honours. He had a brilliant career at Aberdeen University, gaining gold medals for anatomy and one for being adjudged the most distinguished student of his year. He graduated M.B., Ch.B. in 1928, and four years later his thesis for the M.D. brought him the Thursfield Award, which is given for the best thesis of the year. Resolved on a research career in some branch of pathology he went to Paris to continue his training at the Pasteur Institute. Here he worked in the department of Professor Levaditi, studying rat-bite fever and relapsing fever. From Paris he went to the University of Munich to work with Professor Borst, and, returning to this country, he joined the staff of the Imperial Cancer Research Fund, then under the directorship of the late Dr. J. A. Murray. For the first few years that he spent there he made a study of transplantable tumours, a subject which was still in its infancy at that time, but later he joined forces with the late Dr. W. E. Gye, who succeeded Murray as director, and together they tackled the problem of virus-induced tumours. This work he continued after his move to the Middlesex Hospital in 1936, where with the late Professor James McIntosh he was responsible for some outstanding achievements on the nature of virus neoplasia.

The next phase of his work included the war years, and at this time Selbie turned his attention to the urgent problems arising from the discovery of the sulphonamides and the antibiotics. On this subject he made some first-class contributions to the medical literature, among which may be mentioned his work on infective endocarditis and on gas gangrene. In this, close collaboration with the clinician was essential, and his co-operation with the clinical staff of the Middlesex Hospital was an important contributing factor to the great value of this work.

After the war Selbie was called upon to take charge of the bacteriology department of the Middlesex Hospital, and while still continuing with research work his activities found a much wider scope in the assistance he gave to the staff of the Middlesex Hospital and in his great service to the students. He was a brilliant

exponent of his subject and a sympathetic teacher with a full realization of the students' difficulties. He took the degrees of Ph.D.(London) in 1944 and D.Sc. in 1949.

Apart from his contributions to research and his work in the school and hospital, his ability and personality led to his being invited to undertake numerous outside responsibilities. These he carried out with enthusiasm and the same high standard which characterized all his work. He was secretary of the Pathological Section of the Royal Society of Medicine, and latterly was the representative of that Section on the editorial committee. He was also secretary of the Board of Studies in Pathology for four years and acted as examiner in pathology for the final degree. He had been editor of the *British Journal of Experimental Pathology* and assistant editor of the *British Journal of Cancer*. He gave lectures to the nurses of the Middlesex Hospital and also, for the Royal College of Nursing, to the sister tutors; he was in the middle of a course of these lectures at the time of his death. He was an energetic member of the Royal Microscopical Society, of which he was a vice-president, and attended most of its meetings. He was also a member of the Medical Research Club and of the Pathological Society of Great Britain and Ireland. In these numerous activities Selbie was unsparing of himself and rendered considerable service to the world of pathology in general.

His apparent reserve on early acquaintance soon melted on better knowledge of him, and his colleagues have cause to appreciate his great helpfulness and loyalty to them. To his fellows his outstanding characteristic was one of unselfish helpfulness, but he could be very forthright in denouncing slipshod work or specious assertions made with little foundation. He made an excellent companion both in his work and elsewhere. At the height of a brilliant career the tragic death of Selbie at the age of 49 leaves gaps in many circles.—R. W. S. and S. P. B.

EUGENE WOLFF, M.B., F.R.C.S.

Mr. Eugene Wolff, ophthalmic surgeon to the Royal Northern Hospital and to the Moorfields, Westminster, and Central Eye Hospital, died suddenly in London on February 28. He was 57 years of age.

Eugene Wolff was born at Oudtshoorn, Cape Province, South Africa, on March 11, 1896. He was educated in London at University College School and then at University College Hospital. Graduating M.B., B.S. in 1918, he won the Lister medal for clinical surgery in the same year, and was appointed ophthalmic registrar at University College Hospital after he had held the post of house-surgeon there. From 1918–19 he served in France as a captain in the South African Medical Corps, and then returned to University College as demonstrator of anatomy, a post which he held until 1930. Meanwhile he was developing his interest in ophthalmic surgery, and held the post of chief clinical assistant at the Royal London Ophthalmic Hospital. In 1928 he was appointed ophthalmic surgeon to the Royal Northern Hospital. Eight years later he joined the staff of the Royal Westminster Ophthalmic Hospital. He was also at one time ophthalmic surgeon to the Metropolitan Hospital in London.

Besides building up a big practice in his specialty he played an important part in ophthalmological affairs generally, and in 1950 he was appointed by the University of London as a teacher in ophthalmology at the Institute of Ophthalmology. He had held office as vice-president of the Ophthalmological Society of the United Kingdom and also the Ophthalmic Section of the Royal Society of Medicine; and the Belgian and Greek Ophthalmological Societies had honoured him by awarding him honorary membership. Since 1950 he had been a member of the North-west Metropolitan Regional Hospital Board.

Wolff was not only a first-class ophthalmological surgeon, but he had a keen, inquiring mind and an enviable ability to express himself clearly. His early interest in anatomy never left him. One of the earliest of his publications was a book entitled *Anatomy for Artists*, which reached its third edition in 1947. He was also the author of *An Anatomy of the Eye and Orbit* (fourth edition, 1953), *Pathology of the Eye* (third edition, 1951), and *Diseases of the Eye* (fourth edition, 1952). In 1923 he married Lydia Abravanel; she and a daughter survive him.

We are indebted to Mr. P. McG. MOFFATT for the following appreciation: The sudden and unexpected death of Eugene Wolff has deprived ophthalmology of one of its most distinguished exponents. I had the privilege of knowing him from the time of his first association with the then Royal Westminster Ophthalmic Hospital in 1930. His career had already taken shape. A brilliant studentship at U.C.H. had been followed by ten years' study of, and demonstrating, anatomy, pursued at the same time as the study of ophthalmology at his parent hospital and at Moorfields. His love of anatomical detail and the influence of Elliot Smith, Percy Flemming, and Sir John Parsons give the clue to his early devotion to the study of the anatomy, histology, and pathology of the eye. In these fields he earned an international reputation by his original observations and the publication of *An Anatomy of the Eye and Orbit* and *A Pathology of the Eye*: both are accepted standard works to-day. He was a lucid lecturer and a great teacher, possessing infinite patience, anxious and able to impart his knowledge to others. I enjoyed many demonstrations of slides and specimens in the pathological laboratory, where he spent much of his time, and where many of the illustrations for his books were prepared. He had an immensely wide knowledge of ophthalmic literature, a fact well known to his colleagues, who often brought their problems to him and rarely did so in vain. To his juniors he was always encouraging and imbued them with the spirit of enthusiasm to advance the knowledge of their specialty. He used to say that he could read French and German but could not speak either language. On one occasion when he was due to read a paper before the French Ophthalmological Congress he confessed to his friends that it was possible to read the paper in French but that answering questions afterwards was a very different matter. As expected, he acquitted himself with distinction. He wrote a great many papers on subjects of histological, pathological, and clinical interest, and in addition to the two books already mentioned he wrote *An Anatomy for Artists* in 1926, *A Shorter Anatomy* in 1928, and *Diseases of the Eye* in 1937. All his books have gone into several editions. He was for ten years lecturer in anatomy at the Slade School of Art.

To his friends who knew him well, his outstanding qualities were his modesty about himself and his very considerable achievements, his enthusiasm and indefatigable industry, and his kindness. As a recognition of his valuable contributions to ophthalmology he was awarded the William Mackenzie Memorial Medal at Glasgow in 1947. In the preface to his books he paid tribute to the help afforded him by his wife. To her and their daughter we extend our deepest sympathy. Wherever ophthalmologists gather together the name of Eugene Wolff will be remembered.

H. E. L. writes: I should like to add a small tribute to the late Mr. Eugene Wolff. It was my great privilege to have his friendship soon after I arrived in Britain and came

to work at University College. I shall always remember with affection the time spent with the Wolffs at their beautiful home in Wimpole Street. To us—postgraduate students and junior academic people—these were wonderful evenings, full of warmth, human kindness, and cultured conversation. Sir Arthur Keith, in his *Autobiography*, recalls as a young man, living in "digs," how much he appreciated the visits he made to certain friends of his, and that they kept him in touch with "how life should be lived." I felt the same appreciation of Mr. Wolff's hospitality, but he was always embarrassed when I quoted Sir Arthur Keith. One was often tempted to stretch one of their invitations and include a colleague or two who might be currently depressed by impending examinations, or home sickness, or the general physical discomforts of lodgings in Bloomsbury, Notting Hill Gate, or Camden Town. A few hours spent in the lively sympathetic company of Mr. Wolff and his family would restore morale for a long time. Their generosity seemed inexhaustible; they never boggled at the troop that I brought, and somehow or other I was always asked again. An adequate tribute is very difficult, coming from me: it tends to sound trite, and I shall respect his memory by avoiding what he abhorred. I speak on behalf of many of my friends when I extend our deepest sympathies to his family.

H. W. POOLER, M.D.

We record with regret the death on February 28 of Dr. H. W. Pooler at the age of 88. He was elected a Vice-president of the British Medical Association in 1947. In his autobiography, *My Life in General Practice*, he described himself as "an ordinary general practitioner." He certainly showed in that volume that the life of the busy family doctor, ordinary or otherwise, was not lacking in human interest or drama or colourful incident. He showed also that it had its deep and abiding satisfactions.

Henry William Pooler was born at Wellington, Shropshire, on January 30, 1866. His father was a tailor and draper in that town. One of his earliest recollections was of seeing Captain Webb, of Channel-swimming fame, who was the son of a doctor in the neighbourhood, arrive at Wellington, where the people took the horses out of his carriage and dragged it to his hotel. At the age of 10 Pooler was sent to the traditional school of his family, Adams' Grammar School, Newport, in the same county. At 17, having passed the London matriculation, he was firmly resolved on medicine as his career. The difficulty was ways and means. His father had no money to spare. It was arranged that Pooler should become a pupil of his uncle, Dr. George Hollies, a man of sterling character—when approaching his 80th year he went up to Cambridge to take his M.A. degree at the same time as his grand-nephew. This pupilage allowed Pooler to register as a medical student eighteen months before entering a medical school proper, and it gave him an insight into medical practice. In those days there were no telephones and no cars. The doctor, if a call came at night, had to saddle and bridle his horse for riding or harness it to his vehicle for driving, and whatever complications he found when he got to his case he had to deal with them himself. Pooler never ceased to be grateful for an insight into general practice in the country under those conditions. After about eighteen months with Hollies he was entered as a student at Queen's College, Birmingham, in 1885. Later on he returned as a qualified assistant, spending six months with his uncle before taking up a succession of resident hospital posts. During those six months he helped his uncle amputate a thigh and a forearm, while finger amputations, strangulated hernias, and the like were all in the day's work. He would start out on horseback on his country round at about ten in the morning, lunch at a convenient inn, and return home about four in the afternoon; and then perhaps he might have to saddle another horse to visit a patient some miles away. Midwifery calls were frequent. Pooler himself declared much later that he had done every operation in midwifery except caesarean section.

During his student career in Birmingham he served as a dispenser to a doctor in the city. His wages began at 15s. a week and rose to 50s., together with the offer of a partnership by the time he had qualified, but, having his eye at that time on the Indian Medical Service, he declined the offer. He was accustomed to do his dispensing each morning until ten or later, then to rush to the hospital for clinical lectures and ward work, and, in the afternoon, lectures at the college.

He qualified L.S.A. in 1889, and before going up for the last part of his final he obtained the most valuable prize open to senior students at the General Hospital, that of resident medical assistantship. Later he became house-surgeon in the obstetric and ophthalmic department at Queen's, and subsequently was elected to the post of house-physician. Dr. Guy Dain was one of those who, as clinical clerks, came under his more or less paternal eye. It was while at Queen's that Pooler met Sybil Woodward, a nurse, whom he married in 1894, and thus began the happiest of married partnerships, which continued for more than 50 years. Mrs. Pooler died on November 5, 1951. He obtained the London Conjoint diploma in 1890 and took the degrees of M.B., B.Ch. of the University of Birmingham in 1901, proceeding M.D. in 1952, over 50 years later.

On leaving hospital Dr. Pooler bought a practice at Ashted, a district in the east end of Birmingham, for £700, and received in the first twelve months £412. Eventually, however, he made a good income, but the work was very hard—morning and evening surgery at home and at a branch surgery from 8 to 9 p.m. or later, after a long day's visiting, and there were many night calls. Midwifery was essential in those days to the general practitioner, and he averaged over 200 cases a year. After 15 years, tired of the round of practice, he took up a whole-time position as district medical officer and public vaccinator, but when the National Health Insurance Act came in he resolved to get back into private practice. Practice in the east end of Birmingham was not exactly a bed of roses, but one thing on which he always looked back with great satisfaction was the formation of the Birmingham Infant Health Society, of which he was appointed honorary medical officer. It was a gratification to him, many years after he had left Birmingham, to have his old centre chosen on the occasion of a royal visit as a representative example of pioneer child welfare work. For some years Pooler was a member of the Birmingham City Council, and undertook as a member of the housing committee two extensive tours to inspect Continental housing. He also represented the city at international conferences on child welfare at Berlin and Dresden.

His connexion with Birmingham came to an end in 1916, when he took up a practice in the attractive village of Stonebroom, near Alfreton, in Derbyshire. Here the income was small, but the work, though heavy, was congenial and the people friendly and pleasant to serve. After twenty happy years he left this village for the

neighbouring one of Ashover, while his son Alan carried on at Stonebroom, the father still continuing to do some work in the practice. To the great grief of his family and friends, Alan Pooler, always delicate in health as the result of rheumatic fever in early life, died as the result of overstrain during the second world war. Dr. Pooler's other three sons are all members of the medical profession, and his daughter is married to a doctor. The later years of Dr. H. W. Pooler were spent in retirement at Ashover, where his hobbies were alpine gardening, the collection of old English watercolours, music, and the game of chess.

While in practice in Birmingham Pooler was made honorary secretary of the Central Division. There his first duty was to issue 350 confidential circulars to members informing them that certain practitioners had come under the ban of the Association for conduct held not to be in accordance with the honour of the medical profession by acting as medical officers of a certain dispensary in Coventry. That affair ended in a writ for conspiracy, libel, and slander, and heavy damages were awarded against the Association.

On moving to Derbyshire he was again made honorary secretary of the Division, where he found himself plunged into a series of fights with miners' clubs—clubs formed for the purpose of providing miners' dependants with medical treatment—and in a fight with the county council over the salaries of district medical officers. He was elected president of the Midland Branch, and later, when Derbyshire became a Branch by itself, of that Branch also. He was a member and treasurer of the Derbyshire Panel Committee, and the moving spirit of a benevolent trust, the object of which was to make grants to needy Derbyshire insurance practitioners or their dependants, particularly for educational purposes. For many years he was a familiar figure in the Representative Body, and in 1930 he became a member of the Council, where he sat on many committees, but did his chief work as chairman of the subcommittee concerned with maternity and child welfare. He was one of a small committee which went to South Wales to investigate the well-remembered Llanelly dispute in 1934. His term as member of Council ended in 1943, and in 1946 he gave up the local secretaryship. He had then been in the medical profession as student and practitioner for more than sixty years. At the Annual Representative Meeting held in London in July, 1947, he was elected a Vice-President of the British Medical Association as an appreciation of the exceptional services he had rendered to the Association.

Pooler will be recalled as a friendly, vivacious companion, a man with a great faith in his profession and its ideals, and an "ordinary general practitioner" who managed to fill out his length of days with the most devoted service to his fellow-beings and thereby with an amplitude of quiet happiness for himself.

Dr. GEORGE COOPER, who died on November 24, 1953, at Budleigh Salterton, where he had spent many years in retirement, was at one time director of the department of radiotherapy at the General Infirmary at Leeds. He was 75 years of age. Born at Belfast on June 22, 1878, he had a distinguished academic career at Queen's University. He took an arts degree at the Old Royal University of Ireland in 1909, and in 1911 graduated M.B., Ch.B. at Queen's University, gaining not only first-class honours but obtaining first place and being awarded a special exhibition. Two years later he proceeded to the degree of M.D. He held resident appointments at Worcester General Infirmary and at the National Hospital for Nervous Diseases before, during the first world war, he became medical officer in charge of the electrotherapeutic department of the Royal Victoria Hospital at Netley. This appointment was followed, in 1921, by a similar one at the General Infirmary at Leeds, where he was placed in charge of the electro- and radiotherapeutic departments. The following year he obtained the Cambridge D.M.R.E. Dr. Cooper was one of the pioneers of deep *x*-ray therapy, and was unremitting in his efforts to obtain the most up-to-date and powerful apparatus available. His enthusiasm often induced interested philanthropists to buy new apparatus for his department. In 1920 less than 100 patients attended the department, and by 1925 the number of new patients had increased tenfold. He was appointed lecturer in radiology and electrotherapy at Leeds University in 1924. When the British Medical Association held its Annual Meeting at Oxford in 1936 he served as a vice-president of the Section of Physical Medicine. He retired in 1937. George Cooper did his work with a thoroughness and care which were a feature of every aspect of his life. His specialty brought him into contact with large numbers of patients, many of whom were gravely, and often hopelessly, afflicted. He felt deeply for these people, and invariably extended to them a kindliness and sympathy which were as sincere as they were spontaneous; for his quiet, sometimes almost whimsically shy bearing concealed a warm and generous humanity, which was itself the product of a refined and cultured mind. A wide and avid reader, he was keenly devoted to both music and painting, and was as well a true countryman, deeply interested in his garden, and indeed in all aspects of natural beauty. He will be remembered as a delightful professional colleague, a refined and courteous gentleman, and a loyal and trusted friend.—A. W. G.

Dr. ROBERT WILLIAM BOLLANS, who died in hospital at Glossop, Derbyshire, on January 29 at the age of 81, was well known in the district for over half a century. He was born at York and educated at the Yorkshire College, Leeds, graduating M.B., Ch.B. at the Victoria University of Manchester in 1897. Having lived in Derbyshire since boyhood he came to regard Glossop as his home town, although he actually practised from the neighbouring village of Hadfield. From the time he returned to Derbyshire in 1898 as a qualified medical practitioner until his death he was liked and respected by his patients and colleagues as a real family doctor. Always immaculately dressed, and quiet and courteous in manner, he quickly built up a large practice. He was an admirable choice for a justice of the peace, his tolerance and common sense being particularly appreciated in the juvenile court. For many years he was surgeon to Woods Hospital, Glossop, and medical officer to the Hadfield district of the Glossop Union. He had the distinction of being a hereditary freeman of the City of York, his birthplace. A member of the British Medical Association for 53 years, he was secretary of the Glossop Division from 1922 to 1925 and chairman of the Division from 1940 until the time of his death. He had a heart attack on Christmas night last year and was admitted to Woods Hospital, where he died. He leaves a widow, one son, and one daughter.

Dr. DOROTHY STOPFORD PRICE, consulting physician to St. Ultan's Infant Hospital, Dublin, died at her home at Dublin on January 30 at the age of 63. Elinor Dorothy Stopford was born at Dublin in 1890, the daughter of the late Mr. J. J. Stopford, and was educated at St. Paul's Girls' School, London, and at Trinity College, Dublin, graduating M.B., B.Ch. in 1921. She proceeded to the M.D. in 1935. Shortly after graduation she became dispensary medical officer at Kilbrittain, Co. Cork, where she figured prominently during the "troubled times" as the medical officer to a brigade of the I.R.A. When all other means of transport were denied, Dr. Stopford reached her more distant patients in West Cork

on horseback. Early in her career she became associated with St. Ultan's Infant Hospital, Dublin. Other appointments which she held were those of clinical assistant to the children's department, Royal City of Dublin Hospital, consulting physician to the Royal National Hospital for Consumption for Ireland, and consulting physician to the Children's Sunshine Home, Stillorgan, Co. Dublin. In 1925 she married Mr. Liam Price, D.J., who survives her.

J. St. P. C. writes: It was for her work as consultant physician at St. Ultan's Hospital that Dr. Price earned for herself an international reputation. She became attracted by the problem of childhood tuberculosis and devoted herself more and more to this specialty. Directly through her efforts there was built in 1945 at St. Ultan's a unit specially for the treatment of primary tuberculosis. Four years later, in 1949, the B.C.G. unit, another monument to her endeavour, was formally opened at the same hospital. In the City of Dublin to-day and throughout the Irish countryside there are many who owe their lives to her enlightened care of them when, as children, they were brought to her wards at St. Ultan's suffering from the effects of childhood tuberculosis. Her vast experience of the treatment of childhood tuberculosis was frequently drawn upon by Dr. Price for her many scientific contributions to British and Irish medical journals; it was synthesized and published in 1942 in her book, *Tuberculosis in Childhood*, a classic in its subject and a book which to-day enjoys world-wide circulation. In 1937 she began to use B.C.G. vaccine at St. Ultan's Hospital. Advocating its use more widely, she met, inevitably, with considerable opposition, but in the subsequent years she stuck fast to her faith in its powers of prevention and her work did not go unnoticed. In 1949 the Irish Government, as part of a vigorous drive against tuberculosis, decided to launch a national campaign for the use of B.C.G. vaccine. In deference to her pioneering work and to her accumulated experience at St Ultan's Hospital, the Government centred its campaign on her hospital, and the Minister for Health nominated Dr. Price as chairman of the National B.C.G. Committee. She pursued this work with renewed vigour and enthusiasm. Indeed, her illness, which began in 1950, was undoubtedly the result of so much overwork. In the years since 1950, Dr. Price, although physically incapacitated, kept in constant touch with the development of the use of B.C.G. vaccine at home and abroad. From time to time she published results of the work in Ireland, and indeed, until a fortnight before her death, was engaged in the preparation of a paper for publication. In 1951 Dr. Price was nominated by the executive committee of the Irish Medical Association as a candidate for the award of the Leon Bernhard Foundation prize, given by the World Health Organization for practical achievement in social medicine. Her loss will be widely mourned.

Dr. BALFOUR MCKEAN, who was in practice at Sheffield for over 40 years, died suddenly on February 12 at the age of 66. He was educated at Glasgow High School and Glasgow University, where, after a distinguished career as an undergraduate, he graduated M.B., Ch.B. in 1910. Three years later he proceeded to the M.D., being awarded a high commendation for his thesis. His first appointment was that of house-surgeon at Glasgow Royal Infirmary. In 1911 he was for a time assistant medical officer at the Park Hospital, Hither Green, London, when that institution was being used as a hospital for sick children, and then he returned to Glasgow as house-physician at the Western Infirmary. In 1912 he moved to Sheffield, where he held the appointments of assistant medical officer and, later, deputy medical superintendent at Fir Vale Hospital, known since 1930 as the City General Hospital, Sheffield. During the first world war he held a commission as a captain in the R.A.M.C. and was attached to the 3rd Northern General Hospital, of which the 550 military beds at his hospital were a part. After 13 years of whole-time hospital work he decided to enter private practice. He was an active member of the British Medical Association all his professional life and served on the executive committee of the Sheffield Division. He was a medical referee for the Ministry of Health and chairman of No. 2 medical board of the Ministry of Labour and National Service. He also served for a time on the board of governors of the United Sheffield Hospitals. In December, 1940, during the first major air raids on Sheffield, his house suffered a direct hit, and he, his wife, and his daughter were buried under the debris. Fortunately he was a strong man, and was able to lift a girder which lay across his wife's chest and to extricate her and his daughter. A less powerful man would probably have failed and all would have perished, as the debris was then on fire. In spite of severe shock he carried on his work as a practitioner. He was an athlete in his younger days, his favourite sports being tennis and swimming, but in later years pressure of work left him little time for recreation. Eventually work at such high pressure took its toll, and in 1951 he suffered a severe vascular lesion from which he slowly recovered. He was advised to take things easy, but it was not his nature to relax, and soon he was working as hard as ever. On the day of his death he had a very full list of professional engagements, and was on his way home when he collapsed. He was able to drive his car to the side of the road and stop the engine before he died, as he wished, in harness. Dr. McKean was a clinician of exceptional ability and wide experience who never spared himself in any circumstances. He was a staunch friend and loyal colleague and will be sadly missed by his patients, his friends, and his fellow practitioners. Our sympathy goes out to his widow and daughter in their loss.—J. C. and R. C B.

Medical Notes in Parliament

MEDICAL AUXILIARIES' QUALIFICATIONS

The new regulations governing the employment of medical auxiliaries, which come into operation on April 1, were discussed in the House of Commons on February 23. The debate, which arose on a prayer for the annulment of the regulations, was primarily designed to seek information of the Minister's intentions, and to ventilate some doubts, and the motion was withdrawn at the end of it.

Mr. IAIN MACLEOD, Minister of Health, did not offer an enthusiastic defence of the regulations, presenting the procedure adopted as no more than the least undesirable of the courses open to him. He recounted the failure to get agreement on the 1951 suggestions, which were more favourable to medical auxiliaries than the Cope Report from which they originated, and the necessity for taking a decision which faced him at the end of 1952. He could have pushed ahead on the lines of the Cope Report, either on its original basis or as modified, but in face of the known hostility of many of the bodies concerned, including some of the most important, that would have been disastrous. He could, assuming time was available for the necessary legislation, have established statutory registration for each of the groups concerned; the overwhelming objections to that were the necessity for consultation between the groups, and the practical difficulty that many were too small to justify or support financially such a proposal. He could have done nothing, but government by circular was bad, and cases of unfairness were arising as a result of the 1951 circular. So he was left to exercise his powers under Section 66 of the Health Act to lay down qualifications. It was undesirable that the Minister should have to concern himself with qualifications of this kind, and the whole basis of his case was that the regulations were only a temporary measure. He had sent his "rough ideas" to the organizations concerned, and had told them in recent correspondence of his intention to set up a working party to continue the probe to get agreement. He was hopeful of the results. It was important to note that a solution did emerge from

the organizations concerned, partly no doubt as a result of the catalyst of these regulations.

Approval had to be given before April 1 to existing courses of training that were adequate. All the bodies had been asked to send him before the end of February particulars of their courses and examinations. He intended, for the future, to invite those who advised him, assisted by his consultant advisers, to examine the courses and examinations of the representative training schools. Since the discussion had been most closely concerned with physiotherapists, he added that on this he would ask the advice of his consultant adviser, Dr. Cooksey, director of the department of physical medicine at King's, and also of Sir Harry Platt, emeritus professor of orthopaedics at Manchester.

He repeated the assurance that standards that were too low would not be accepted, and quoted from the *British Medical Journal* annotation of February 6 (p. 325):

"There is now undoubtedly an opportunity for the Minister to achieve a piece of constructive statesmanship which will bring the position of medical auxiliaries into line with the other professions in the National Health Service."

This is what he would like to achieve. This was a temporary measure. He would do his best to reach a final solution. In the consideration of standards he would first be guided by the findings of the Cope Committees, and would then act on the best advice available to him.

Dollars for Cardiac Delegation

Lord CROOK asked on February 23 whether the Treasury had reconsidered the application of the British Cardiac Society for permission to send a larger number of delegates to the World Conference on Cardiology in Washington next September, and, if so, with what result. Lord HAWKE, Lord-in-Waiting, replied that after full consideration the Treasury had allowed currency for the full number of delegates applied for—namely, 32.

Prescription Charge Claims

Mr. OSBERT PEAKE, Minister of Pensions and National Insurance, informed Mr. A. BLENKINSOP on February 22 that it was estimated that in the calendar year 1953 Assistance Board grants in respect of Health Service charges amounted to about £1,060,000, of which prescription charges account for about £445,000 and dental charges about £235,000.

Typhoid-infected Cream

Mr. IAIN MACLEOD, Minister of Health, in a statement on February 22 on the search for tins of cream suspected of being infected with typhoid, said that from information supplied by the manufacturers and importers medical officers of health were informed of the location of wholesalers and retailers as soon as their names could be ascertained. Although at that stage he could obviously make no predictions, he could say that up to that date no case of typhoid attributable to this cream had been notified.

Mr. T. STEELE asked on February 25 if the Minister was prepared to use his powers to prevent the import of tinned foods from Ireland pending proper investigations. Miss PAT HORNSBY-SMITH, the Parliamentary Secretary, replied that the Minister did not think the circumstances called for this.

Supplementary Ophthalmic Services

Mr. SOMERVILLE HASTINGS asked the Minister of Health on February 25 whether, in order to save time, he would give instructions to ophthalmic opticians providing supplementary ophthalmic services under the National Health Service Act to refer cases needing further investigation direct to ophthalmic surgeons, at the same time notifying the general practitioner in charge of the case. Miss PAT HORNSBY-SMITH, Parliamentary Secretary, replied "No." It was for the general practitioner to decide whether a patient required specialist treatment, which would not always be that of an ophthalmologist. The Minister had no evidence that this caused needless delay.

Medico-Legal

PLOT TO DEFRAUD HEALTH SERVICE

A doctor and a chemist were each sentenced to prison for one year by Mr. Justice Sellers at Essex Assizes on March 1. They had been found guilty of conspiring together to defraud the Essex Executive Council of the National Health Service, and causing to be paid to the firm of which the chemist was managing director, by false pretences with intent to defraud, cheques for £1,121 6s. 8d., £1,392 18s. 1d., and £826 16s. 7d. The doctor was Archibald Luke Basham, aged 49, of Rayleigh, Essex, and the chemist Geoffrey William Unwin, aged 38, managing director of Yardley (Rayleigh), Ltd. They had pleaded not guilty.

The prosecution contended that Basham wrote out some prescriptions, and that Unwin collected the money from the paying authority of the National Health Service on the basis that the articles mentioned on the prescription had been supplied from his shop, whereas in some cases the articles had not been received by the patients. It was not suggested that the whole of the large sums mentioned in the charges represented drugs that were not supplied, but that a portion represented drugs and other articles not supplied. It was said for Unwin that only 2% of the sums mentioned in the charges were actually involved.

Both men gave evidence strongly denying any dishonest intent. They said that, although there might have been some irregularities, there was certainly no dishonesty or any attempt to obtain any money by false pretences.

Patients of Dr. Basham were called, one of whom described him as "a thoroughly satisfactory and painstaking doctor."

Detective-Sergeant L. H. Chaplin stated that in 1941 Basham, then an R.A.F. medical officer, had been convicted at a court martial for drawing drugs for his own use and neglecting to record prescriptions. He was sentenced to be dismissed the Service, but this was commuted to a severe reprimand. He afterwards resigned from the Service. Before the war he had been a house-surgeon at several hospitals. Sergeant Chaplin agreed that the doctor had been a voluntary patient in a mental hospital for seven weeks last autumn, and that he was now practically penniless. He was unmarried. He first went into practice on his own in 1950.

Unwin, married, with one child, had no previous convictions.

The Judge said it was apparent that the National Health scheme required the utmost honesty on the part of those engaged in it as medical practitioners or chemists, because the prescription was a thing of value. If the ingredients on it were dishonestly increased, the value was increased, and this increased the amount to be paid to the chemist. While the increases might be small in relation to this particular case, it opened up an avenue of continued and successive fraud against the system, and this had to be paid for by the public.

The Judge said that he would take into consideration the fact that Basham had been in a mental hospital, and had been in custody since December, and treat both men equally. The basis of the allegation against the two men, he said, was that they had used bogus prescriptions. He told the jury that Dr. Basham appeared to be a quite skilled, qualified doctor who attended to his duties quite diligently, and no one was suggesting that Unwin was not a qualified chemist or that he was unskilled or careless. The allegation was that they had been dishonest. The heart of the case was that the prescriptions were at times for drugs which were never dispensed and never supplied. Therefore there was a demand for money to which the chemist was

not entitled. Or perhaps there might be a lesser view, the Judge continued, that at times part, but not all, of the drugs prescribed were dispensed. The defence had said that the doctor had dispensed drugs at his surgery and later sent prescriptions to the chemist to replenish his stock, and they asked the jury to say that they might have been irregular and careless. If the jury thought that was all, and nothing more, then they would acquit them.

Vital Statistics

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in January, 1954, was 132, compared with 116 in the previous month and 100 (revised figure) in January, 1953.

The number of cases of industrial diseases in the United Kingdom reported during January was as follows: lead-poisoning, 4; other poisoning, 0; anthrax, 2; epitheliomatous ulceration, 6; and chrome ulceration, 28; total, 40. There was one death from anthrax.

The number of persons killed during the 13 weeks ending December 26, 1953, as a result of accidents occurring in that period at mines as defined by the Coal Mines Act, 1911, in Great Britain was 87, compared with 86 in the 13 weeks ending September 26, 1953, and 107 (revised figure) in the 13 weeks ending December 27, 1952. The corresponding numbers of persons seriously injured at such mines were 475, 445, and 598 (revised figure).—*Ministry of Labour Gazette*, February, 1954.

Week Ending February 20

The notifications of infectious diseases in England and Wales during the week included pneumonia 932, scarlet fever 1,223, whooping-cough 2,099, diphtheria 19, measles 1,944, dysentery 754, acute poliomyelitis 19, paratyphoid fever 10, and typhoid fever 1.

Infectious Diseases

Only relatively small changes occurred in the trends of the notifications of infectious diseases in England and Wales during the week ending February 13. The largest fluctuations were increases of 359 for measles, from 1,487 to 1,846, 146 for scarlet fever, from 1,015 to 1,161, and 45 for dysentery, from 624 to 669, and a decrease of 68 for whooping-cough, from 1,984 to 1,916.

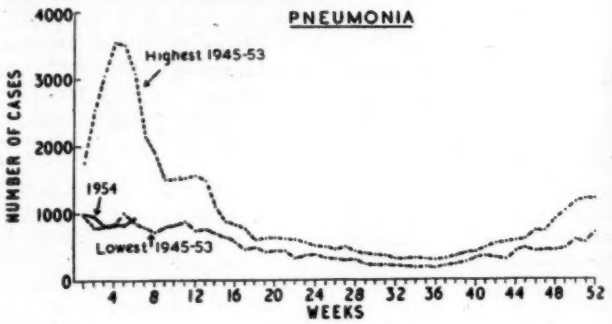
The increase in the incidence of measles was concentrated in the northern section of the country. The largest rises were 103 in Lancashire, from 262 to 365, 47 in Yorkshire West Riding, from 61 to 108, and 40 in Cumberland, from 160 to 200. The rise in scarlet fever was mainly contributed by the south-eastern and midland counties; the largest rise was 30 in Kent, from 35 to 65. The largest rises in the local trends of whooping-cough were 31 in London, from 45 to 76, and 31 in Yorkshire West Riding, from 141 to 172. 11 cases of diphtheria were notified, being 8 fewer than in the preceding week. The chief features of the returns of diphtheria were a rise of 0 to 3 in Middlesex and a fall from 3 to 0 in Warwickshire.

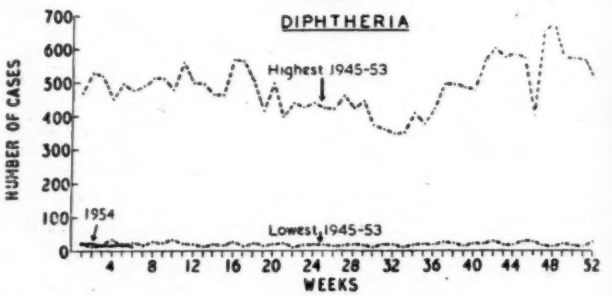
21 cases of acute poliomyelitis were notified, and these were 2 fewer for paralytic and 2 more for non-paralytic cases than in the preceding week. The largest returns were London 3 and Gloucestershire 3 (Bristol C.B. 3).

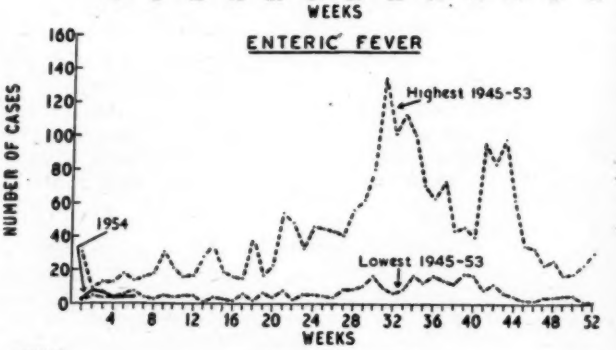
For the fifth consecutive week the incidence of dysentery has risen and the number of notifications is now double what it was five weeks ago. The largest centres of infection during the week were Lancashire 132 (Preston C.B. 37, Bolton C.B. 13, Oldham C.B. 10, Eccles M.B. 10), Yorkshire West Riding 114 (Leeds C.B. 47, Bradford C.B. 37), London 100 (Islington 34, Hackney 26, Wandsworth 10), Middlesex 61 (Enfield U.D. 19, Ealing M.B. 10), Staffordshire 33 (Cannock U.D. 26), Nottinghamshire 24 (Worksop M.B. 16), Norfolk 23 (Norwich C.B. 22), Warwickshire 21 (Birmingham C.B. 20), Essex 18, Kent 17, Durham 17, Leicestershire 17 (Leicester C.B. 12), and Sussex 16 (Brighton C.B. 16).

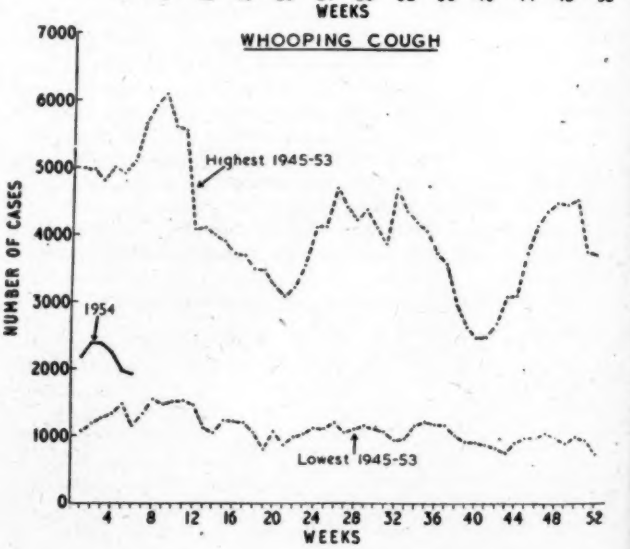
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1945–53 are shown thus - - - - - - -, the figures for 1954 thus ———. Except for the curves showing notifications in 1954, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **February 13** (No. 6) and corresponding week 1953.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	11	0	7	2	3	24	1	13	0	2
Dysentery	669	100	186	6	3	320	36	113	16	1
Encephalitis, acute	1	0	3	0		4	0	0	1	
Enteric fever:										
Typhoid	0	0	0	0	2	4	0	0	0	1
Paratyphoid	4	0	1	0		6	0	1 (B)	0	0
Food-poisoning	109	12		0		40	6		0	
Infective enteritis or diarrhoea under 2 years				15	21				12	14
Measles*	1,849	16	52	28	356	32,359	1507	372	76	293
Meningococcal infection	40	2	11	2	2	53	2	19	2	3
Ophthalmia neonatorum	27	3	5	0		28	2	7	0	
Pneumonia†	931	38	252	10		2,431	228	306	33	10
Poliomyelitis, acute:										
Paralytic	15	2	4	0	6	15	2	0	1	4
Non-paralytic	6	1				1	0			
Puerperal fever§	280	38	13	2		294	33	18	1	
Scarlet fever	1,161	44	202	39	27	1,515	61	247	34	82
Tuberculosis:										
Respiratory	787	70	117	33				170	25	
Non-respiratory	117	4	33	3				29	3	
Whooping-cough	1,916	76	366	74	34	2,238	96	196	34	116

DEATHS in Great Towns	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	1	0	0	0	0	0	0	0	0	0
Dysentery	1	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	13	0	4	1	1	8	2	3	4	1
Influenza	41	8	6	0	3	530	111	3	3	3
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		1	1				1	2		
Pneumonia	495	74	30	8	15	802	158	22	12	11
Poliomyelitis, acute	0	0			0	2	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	133	6	22	2	5	184	35	18	6	10
Non-respiratory		0	0	0	0		4	0	0	2
Whooping-cough	0	0	0	0	0	6	2	0	0	2
Deaths 0–1 year	297	27	37	7	25	293	37	31	11	24
Deaths (excluding stillbirths)	7,982	1207	747	147	243	9,102	1579	644	111	199
LIVE BIRTHS	7,756	1154	899	221	413	6,926	1045	880	155	364
STILLBIRTHS	228	24	23			181	28	19		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

"The London" at Home.—During the last six years the London Hospital, Whitechapel, has expended much thought and money on reorganizing its out-patient department. With 700,000 attendances each year—some 2,000 a day—the London has the largest out-patient department in the country. The whole building, with its 40 departments, has been modernized and redecorated. The new departments—the genito-urinary and gynaecological in particular—are models from the staff point of view of designed efficiency and give greater comfort and privacy for the patients. An appointments system has been arranged and the medical records department has been reorganized. A questionary was sent out recently to 800 general-practitioner "clients" to obtain their criticisms and suggestions from the consumer angle. This was followed up on Wednesday, February 24, when these doctors were invited to an evening At Home in the out-patients department. In addition, members of the lay press were present. Here in an informal atmosphere the hospital staff—consultants, sisters, registrars, and residents—talked with their guests and showed them round. Many who had till then been but a voice on the 'phone or a signature on a letter became realities to each other and, as is usual after such human contacts, felt the better for it.

Poliomyelitis Vaccine.—According to a report last week in the *New York Times*, Dr. J. E. Salk and his colleagues from Pittsburg University, U.S.A., have started to inoculate local schoolchildren against poliomyelitis. This is said to be the first large-scale trial of Dr. Salk's vaccine (see *Journal*, April 11, 1953, page 826), which is said to contain the three main types of poliomyelitis virus. The children are between the ages of 6 and 9 years, and the aim is to inoculate 5,000 of them. From Australia comes the report that the Queen and the Duke of Edinburgh have also been inoculated against the disease, though whether with gamma globulin or a virus-containing vaccine has not been stated.

Medical Education in Manchester.—The ripples caused by last year's World Conference on Medical Education are now becoming apparent. The February issue of the *Manchester University Medical School Gazette* is devoted to a symposium on the education of the medical student, to which a general practitioner and no fewer than seven of the faculty's professors have contributed. In addition there are accounts of medical education in Australia and Sweden, and as an introduction to the symposium a brief summary of the proceedings of the First World Conference is given. What lends special cogency to these essays is the fact that the Manchester curriculum is just now about to be extensively revised, and medical educators elsewhere will welcome the views of their Mancunian colleagues on this very thorny problem. The *Gazette* is obtainable from the Treasurer, *Manchester University Medical School Gazette*, the University, Manchester, 13.

Report on Homosexuality.—The Church of England Moral Welfare Council has issued for private circulation and comment an interim report on homosexuality. The report is the work of a small group of Anglican clergy and doctors, with legal advice, and they alone are responsible for the views expressed in it. Limited to a consideration of the male homosexual, the report discusses the clinical patterns, predisposing and precipitating causes, moral and religious aspects, and the law. At the end are tables of police statistics from 1926 to 1952. That current public anxiety might lead to ill-conceived measures of repression is recognized, and the report seeks to clear the air by a calm statement and examination of the facts. These, in the view of its authors, are of sufficient importance to deserve a full official inquiry. The report is available from the Church of England Moral Welfare Council (price 2s. 6d.) to all concerned with the problem of homosexuality, and com-

ments on it should be sent to Canon H. C. Warner, Church of England Moral Welfare Council, Room 252, Church House, Westminster, London, S.W.1.

B.M.A. Film Library.—The Association is seeking to enlarge and improve its Film Library. The Film Committee would therefore be glad to have details of any recently produced medical films, and to know whether they may be borrowed for appraisal. Information should be sent to the secretary of the Film Committee, B.M.A. House, Tavistock Square, London, W.C.1.

Dr. David Nabarro.—Dr. David Nabarro was 80 years old on February 27. On Monday evening this week Dr. Bernard Schlesinger, the senior physician at the Hospital for Sick Children, Great Ormond Street, presented Dr. Nabarro with a pair of eighteenth century Sheffield plate tea-caddies, an eighteenth century Nanking teapot, an eighteenth century Crown Derby cup and saucer of exquisite design, and a modern tea alarm. Dr. Nabarro was appointed bacteriologist in 1912 and later director of the pathological department, being the first so named in any department of the hospital. He started the first V.D. clinic in the hospital in 1917 and later initiated the biochemical laboratory. His contribution in 1903 in Uganda to the discovery of the trypanosome as a cause of sleeping sickness is now commemorated in the annals of the history of medicine. His book on congenital syphilis, to be published soon, will add further laurels to a name so long held in esteem among paediatricians and pathologists.

Dr. Douglas Guthrie, lecturer on history of medicine, University of Edinburgh, who is returning home from New Zealand and Australia, will deliver the Clendening Memorial Lectures at Kansas City on March 24 and 25, and the Woodward Lecture at the Medical School of Yale University on May 5.

Dr. J. P. M. Tizard, assistant director at the paediatric unit at St. Mary's Hospital Medical School, has been appointed to the University Readership in Child Health tenable at the Institute of Child Health.

Dr. H. J. Gibson, at present medical officer to that part of the University of St. Andrews which is in Dundee, has been appointed to the new post of assistant to the Dean of the Faculty of Medicine, Edinburgh University. Dr. Gibson, who is 43, was previously in the Indian Medical Service.

Dr. J. W. Thompson, research assistant in the department of applied pharmacology at University College Hospital Medical School, London, has been appointed lecturer in the department of pharmacology of the Royal College of Surgeons.

COMING EVENTS

Willesden General Hospital Medical Society.—The inaugural meeting of this society will be held on March 17 at 8.45 p.m. in the department of physical medicine. The meeting is open to all practitioners in the neighbourhood. The subject for discussion will be "The Medical and Surgical Aspects of Thyrotoxicosis." Further information may be obtained from the honorary secretary of the society, Dr. Alec Wingfield, the Willesden General Hospital, Harlesden Road, London, N.W.10.

Ergonomics Research Society.—The fourth annual conference will be held from April 5 to 8 at Ashorne Hill, near Leamington Spa. The theme of the conference will be "The Scientific Study of Human Work in Industry." Sir George P. Barnett, H.M. Chief Inspector of Factories, will speak at the opening session, at which Sir Frederic Bartlett, F.R.S., will be chairman. Further information may be obtained from Miss B. G. Murrell, Slaters Cottage, Peppard Common, near Henley-on-Thames, Oxfordshire.

International Poliomyelitis Congress.—The third international poliomyelitis conference will be held in Rome from September 6 to 10. Further information may be obtained from the secretariat of the conference, Via Lucullo 6, Rome.

British Association of Sport and Medicine.—The annual general meeting will be held on March 19 at 5 p.m. at the Westminster Hospital Medical School, Horseferry Road, London, S.W.1. This will be followed by a paper by Dr. J. L. Blonstein on "Some Medical Aspects of Boxing."

St. Thomas's Hospital Musical Society.—A concert will be held on March 15 at 8.15 p.m. at St. Sepulchre's Church, Holborn Viaduct. No tickets are required.

C.M.F./M.E.F. Physicians' Reunion.—The annual dinner will be held at Simpson's-in-the-Strand on April 10, with Dr. D. Evan Bedford in the chair. Further information may be obtained from the honorary secretary, Dr. A. Willcox, 59, Harley Street, London, W.1.

Dr. A. H. Douthwaite will deliver the Harveian Lecture to the Harveian Society of London at the Royal College of Surgeons on March 16 at 8 p.m. The title of the lecture is "The Problem of Duodenal Ulceration."

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Monday, March 8

INSTITUTE OF NEUROLOGY.—5 p.m., Dr. W. R. Bett: Preparation and Writing of Papers for the Medical Journals.
INSTITUTE OF PSYCHIATRY.—5.30 p.m., lecture-demonstration by Dr. E. Stengel.
MEDICAL SOCIETY OF LONDON.—8.30 p.m., meeting of Fellows. Clinico-pathological Meeting.
UNIVERSITY COLLEGE LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, 4.45 p.m., public lecture by Professor F. Lynen (Munich): Participation of Coenzyme A in the Metabolism of Fat.

Tuesday, March 9

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 7.30 p.m., annual general meeting, followed by a discussion: The Royal Hospital and the Chelsea Pensioners, to be opened by Captain C. J. T. Dean.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. P. J. Hare: Xanthoma Necrobiosis Lipoidica and Granuloma Annulare.
LONDON UNIVERSITY.—At University College Hospital Medical School, 5 p.m., special university lecture in Dentistry by Professor J. Dankmeijer (Leyden): Early Differentiation of Nasal and Buccal Cavities in Relation to Tooth Development.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Mr. A. J. Wrigley: Problem of Postmaturity
WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Mr. J. Minton: Ocular Manifestations in Nervous Disease. Part II.

Wednesday, March 10

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Treatment of Mycotic Diseases.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—6 p.m., Professor Gösta Dohlman (Lund): Mechanism of Vestibular Fistula Reaction.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Dr. S. B. Osborn: Radiotherapy.
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.15 p.m., special university lecture in Physiology by Professor E. A. Müller (Dortmund): Man at Work, a Physiological Analysis.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Sir Cecil P. G. Wakeley, F.R.S., P.R.C.S.: Health of a Nation.
ROYAL SANITARY INSTITUTE.—2.30 p.m., discussion: Tuberculosis: Problems of Notification and Rehabilitation. To be opened by Dr. H. J. Trenchard and Dr. P. W. Edwards.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. S. A. MacKeith: Lecture-demonstration in Psychiatry.

Thursday, March 11

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, W., 8 p.m., Dr. R. R. Bomford: A General Practitioner Looks at Psychosomatic Medicine.
● INSTITUTE OF CHILD HEALTH.—5.30 p.m., Dr. D. A. Pond: The E.E.G. in the Neuro-psychiatry of Childhood.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. O. Oliver: Animal Parasites of the Skin.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5 p.m., Professor F. C. Ormerod: Types of Deafness.
LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Professor D. T. Robinson: Dust as a Possible Source of Infection in Neonatal and Post-operative Tetanus; Dr. T. Black: Role of the Spleen in Thrombocytopenic Purpura.
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.15 p.m., special university lecture in Physiology by Professor E. A. Müller (Dortmund): Man at Work, a Physiological Analysis.
NUFFIELD ORTHOPAEDIC CENTRE.—At Wingfield-Morris Orthopaedic Hospital, Headington, Oxford, 8.30 p.m., Mr. H. Osmond-Clarke: Cervical Spondylosis.
OXFORD UNIVERSITY.—At Southfield School, Glanville Road, Cowley Road, Oxford, 8 p.m., Dr. A. G. M. Weddell: Science and Medicine.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor F. W. Holdsworth: Traumatic Paraplegia.
ST. ANDREWS UNIVERSITY.—At Physiology Department, Dundee, 5 p.m., Professor G. L. Montgomery: Biology of Repair.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., neurology demonstration by Dr. J. H. Paterson.

Friday, March 12

INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. P. J. Hare: Xanthoma Necrobiosis Lipoidica and Granuloma Annulare.
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.15 p.m., special university lecture in Physiology by Professor E. A. Müller (Dortmund): Man at Work, a Physiological Analysis.
MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—At Royal Army Medical College, 5.30 p.m., address to Metropolitan Branch, Society of Medical Officers of Health. Non-specific Urethritis. Opening speakers, Mr. A. H. Harkness and Dr. C. S. Nicol.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Mr. N. C. Tanner: Present Position of Definitive Surgery for Peptic Ulcer.
ROYAL MEDICAL SOCIETY, Edinburgh.—8 p.m., Valedictory Address by the Senior President.

Saturday, March 13

INSTITUTE OF ORTHOPAEDICS, Royal National Orthopaedic Hospital, Stanmore.—10 a.m., Mr. J. A. Cholmeley: Teaching Ward Round.
MIDLAND TUBERCULOSIS SOCIETY.—At Birmingham Chest Clinic, 3 p.m., Dr. J. Pepys: Relationship of Non-specific and Specific Factors in the Tuberculin Reaction.

APPOINTMENTS

BOLZ, ISTVAN ANDRAS, M.D., D.P.H., Medical Officer of Health, Maesteg Urban District Council.

JACK, JOHN B., M.B., Ch.B., Assistant Medical Officer of Health, County of Perth.

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—A. S. Walker, L.R.C.P.Ed., D.L.O., Ear, Nose, and Throat Surgeon (Consultant), Royal London Homoeopathic Hospital, Great Ormond Street; R. L. G. Dawson, F.R.C.S., Assistant Plastic Surgeon (Consultant), Mount Vernon Centre for Plastic Surgery, Northwood; P. E. Baldry, M.B., B.S., M.R.C.P., Physician (Consultant), Ashford Chest Clinic, Ashford, Middlesex; M. W. Hutchings, M.B., Ch.B., Assistant Pathologist (S.H.M.O.), St. Charles' Hospital, Ladbroke Grove; S. K. Ganczakowski, M.B., Ch.B., Assistant Anaesthetist (S.H.M.O.), Bedford General Hospital; Faith C. Poles, M.B., B.S., M.R.C.P., Assistant Chest Physician (S.H.M.O.), Pinewood Hospital, Wokingham; B. Bradley, M.D., D.O.M.S., Assistant Ophthalmologist (S.H.M.O.), Central Middlesex Hospital, Acton Lane, N.W.; D. H. Bodger, M.B., B.S., D.M.R.D., Diagnostic Radiologist (Consultant), West Middlesex Hospital, Isleworth; Mildred I. Pott, M.B., Ch.B., D.C.H., D.P.M., Psychiatrist-in-charge (Consultant), "High Wick" Centre, St. Albans; A. T. Fripp, M.B., B.Ch., F.R.C.S., Orthopaedic Surgeon (Consultant), Heatherwood Hospital, Ascot; Margaret T. Collins, M.B., B.S., D.C.H., D.P.M., Psychiatrist (Consultant), Child Guidance Training Centre, Osnaburgh Street; E. Zwiefach, M.D., F.R.C.S., D.L.O., Ear, Nose, and Throat Surgeon (Consultant), West Middlesex Hospital, Isleworth; P. R. N. Kerr, M.B., B.S., F.R.C.S., Assistant Orthopaedic and Accident Surgeon (Consultant), Luton and Dunstable Hospital; H. D. L. Campion, M.B., B.Chir., Resident Medical Officer (S.H.M.O.), Mount Vernon Hospital, Northwood; C. E. Bagg, M.R.C.S., L.R.C.P., D.P.M., Assistant Psychiatrist (S.H.M.O.), Three Counties Hospital, Arlesey; Ruth A. Cohen, M.B., Ch.B., D.P.M., Assistant Child Psychiatrist (S.H.M.O.), Hill End Clinic, St. Albans; Olive N. Roper, M.B., B.S., Assistant Child Psychiatrist (S.H.M.O.), Hill End Clinic, St. Albans; C. A. G. Cook, M.C., G.M., F.R.C.S., D.O.M.S., Ophthalmic Surgeon (Consultant), West Middlesex Hospital; N. S. Slater, M.B., B.S., F.R.C.S., Assistant Surgeon (Consultant), Edgware General Hospital; J. F. Azzopardi, M.D., Assistant Physician in Geriatrics (S.H.M.O.), Barnet General Hospital; G. W. Csonka, M.D., M.R.C.P., Venereologist (Consultant), Male V.D. Clinic at Shrodells Hospital, Watford; J. C. Ballantyne, F.R.C.S., D.L.O., Ear, Nose, and Throat Surgeon (Consultant), Royal Northern and Highlands Hospital; J. R. Hudson, F.R.C.S., D.O.M.S., Ophthalmic Surgeon (Consultant), Mount Vernon Hospital, Northwood; Jean M. Laidlaw, M.B., Ch.B., D.P.M., Assistant Psychiatrist (S.H.M.O.), St. Bernard's Hospital; W. K. Schnarr, M.R.C.S., L.R.C.P., D.P.H., D.P.M., Assistant Psychiatrist (S.H.M.O.), Friern Hospital.

TATLOW, W. F. T., M.D., F.R.C.P.C., M.R.C.P., Clinical Assistant, Montreal Neurological Institute, and Lecturer in Neurology, McGill University.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Brown.—On February 26, 1954, to Ruth (formerly Richardson), F.R.C.S.Ed., wife of Dr. R. W. W. Brown, South Collingham, Newark, Notts, twin sons.
Gordon.—On February 20, 1954, at 27, Arlington Drive, Ruislip, Middlesex, to Valerie, wife of Neil Gordon, M.D., M.R.C.P., a son—Keith Gray.
Jones.—On January 21, 1954, at the Royal Infirmary, Cardiff, to Dr. Vera Jones, wife of Dr. Idris G. Jones, a daughter.
Law.—On February 23, 1954, at the London Hospital, London, E., to Beryl (formerly Dyson), wife of W. Alexander Law, F.R.C.S., a sister for Bruce—Alison Margaret.

DEATHS

Brown.—On February 14, 1954, at his home, Buckland House, Esher, Surrey, William Brown, M.B., Ch.B., aged 64.
Crawford.—On February 9, 1954, at Gamlingay, Cambs, Jane Crawford, L.M.S.S.A., of Angmering-on-Sea, Sussex, late of Knebworth, Herts, aged 71.
Croucher.—On February 1, 1954, at his home, Chiltern Rise, Woodcote, Reading, Berks, Alexander Henry Croucher, M.D., F.R.C.S.Ed., aged 90.
Curran.—On February 6, 1954, at The Vicarage, Saxton, Yorks, Patrick Joseph Curran, M.B., B.Ch., late of Pudsey, Yorks, aged 57.
Dalling.—On February 1, 1954, Reginald Ramsdale Dalling, M.R.C.S., L.R.C.P., M.R.C.V.S., Major, R.A.V.C., T.A., of Bryn Castell, Caergwele, North Wales, aged 60.
Emerson.—On January 28, 1954, at his home, Chalet Alpina, Vennes-sur-Lausanne, Switzerland, Ambrose Emerson, M.D., aged 78.
Fraser.—On February 8, 1954, at 91, Back Hilton Road, Aberdeen, George Hudson Fraser, M.B., Ch.B., D.P.M., Colonel, I.M.S., retired, aged 63.
Haydon.—On February 2, 1954, at Kingston Hospital, Kingston-on-Thames, Surrey, Walter Turner Haydon, M.R.C.S., L.R.C.P., Surgeon-Captain, R.N., retired, of 221, Sheen Lane, London, S.W., aged 77.
Hill.—On January 29, 1954, at his home, "Dalestead," Caterham, Surrey, Frederick Theophilus Hill, M.C., M.R.C.S., L.R.C.P.
Hoskin.—On February 27, 1954, at his home, London, W., Theo Jenner Hooper Hoskin, M.D., F.R.C.P., aged 65. A memorial service will be held on Thursday, March 11, at Holy Trinity Church, Marylebone Road, at 12.30 p.m.
Kinsley.—On January 29, 1954, Sylvia Victoria Kinsley (formerly Elman), M.R.C.S., L.R.C.P., D.P.H., of Brighton, Sussex.
Stevenson.—On February 3, 1954, at "Redcroft," Meols Drive, Hoylake, Cheshire, Edgar Stevenson, M.D., aged 85.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Straight Leg Raising Test

Q.—*What exactly does the straight leg raising test measure, and how should it be interpreted? How should the test be performed?*

A.—Straight leg raising tests the mobility of the fifth lumbar or first sacral nerve root: thus, if a disk prolapse lies under it, stretching the leg would pull the nerve down and cause pain by increasing the tension. It is therefore a very good diagnostic test for the presence of a disk prolapse, and also a very good measure of the size of the prolapse. It is found that very limited straight leg raising is almost pathognomonic of a large disk prolapse. Clearly, however, adhesions of the nerve root due to inflammation or scarring from an old disk prolapse or post-operative adhesions will also cause pain on stretching. Finally, some patients have tight hamstrings and this will limit straight leg raising, but that does not usually cause severe pain, and is the same on both sides.

The straight leg raising test is usually performed with the patient lying on the back, and each leg is elevated with the knee straight until pain is just caused. It is essential to watch the pelvis, as this may rotate and give a false impression of the freedom of elevation. A refinement of the test is that, when pain just begins, if the foot is dorsiflexed pain will be increased, as this causes further pull on the nerve roots.

Metal Containers for Chloroform

Q.—*Are there any objections to storing chloroform in metal containers similar to those in which trichlorethylene is supplied?*

A.—The manufacturers of one well-known brand of chloroform recommend that chloroform should not be stored in tins. The tins are affected and the chloroform is therefore suspect so far as anaesthetic use is concerned. For this reason, chloroform, including that for export to the Tropics, is packed in bottles.

Boy with a Small Penis

Q.—*The penis of a boy of 12 has hardly increased in size since babyhood, and it is very small. Puberty has not begun. What treatment is recommended? Should treatment be started before puberty, or is it better to wait until then?*

A.—Assuming that the penis is really small and not hidden by fat and that the testes are smaller than one might expect at this age, the more obvious diagnosis would rest between infantilism (of pituitary origin) or eunuchoidism. In the absence of assays of F.S.H. (follicle-stimulating hormone) the differential diagnosis at this age may be difficult, but a positive response to gonadotrophins—for example, chorionic gonadotrophin, 500 units twice weekly for six weeks—would indicate a primary pituitary defect. There would be no response in the case of eunuchoidism, and the appropriate treatment for this latter condition is testosterone or methyl testosterone.

No information is given about height, bone age, muscular development, or adiposity, all of which are relevant to diagnosis and treatment. The age of 12 is near enough to chronological puberty to justify therapy if such is sought by the patient or his parents.

Oestrogens for Prostatic Cancer

Q.—*What is the optimum dosage of stilboestrol in cases of carcinoma of the prostate, and is there any advantage or danger in giving such massive doses as 100 mg. thrice daily? What survival rates are usual after treatment with stilboestrol, and how do they compare with untreated cases?*

A.—There is no general optimum dose of stilboestrol for carcinoma of the prostate; it varies with the individual. It is a good practice to start with 1 mg. three times daily, increasing by 1 mg. each day up to 5 mg. thrice daily by the fifth day. Thereafter the dose is continued, increased, or diminished according to the response. Doses up to 100 mg. thrice daily are usually well tolerated and often have a better effect than smaller doses in refractory cases. There appears to be no danger. It is always better to do a subcapsular orchidectomy as well as giving stilboestrol, and smaller doses may then suffice.

Patients have survived for from 5 to 10 years when oestrogens are combined with surgical measures. Before stilboestrol a survival of three years was considered good.

Severe Myopia in Motorists

Q.—*Do persons with moderate or severe myopia have difficulty in judging distances and thus become potentially dangerous drivers? Is this disability entirely eliminated by correcting glasses?*

A.—There is no sharp dividing-line between moderate and severe myopia, but it is generally true that anything up to 10 dioptres is unlikely to be a severe handicap in driving, provided that appropriate spectacles are worn and the eyes are healthy in other respects. When the myopia exceeds 10 dioptres in amount, peripheral vision is necessarily curtailed by the powerful correcting lenses, but, even so, many high myopes manage to drive well by exercising special care. One source of confusion in driving arises from sensitivity to the glare of headlights, and there is no doubt that the average myope is more readily dazzled than are those who are not short-sighted; and macular disturbances afflict many high myopes, especially in later life. Mobile vitreous opacities are also prevalent. Any of these three pathological states can of course lead to intense confusion in driving, but their detailed consideration is beyond the scope of the query.

Dating the Menopause by the Menstrual Cycle

Q.—*Is there any correlation between the length of a woman's menstrual cycle and her reproductive period of life? For example, does a woman who menstruates every 23 days or so have an earlier menopause than the average?*

A.—The idea behind this question, presumably, is that if a woman uses up her allotted number of ova more quickly than average the menopause will occur earlier. Another popular notion with a similar background is that each pregnancy (during which ovulation is suppressed) postpones the age of the menopause. The basis for such views is unsound, because it is doubtful whether the menopause is the result of the ovary coming to the end of its supply of ova. And, even if this is the case, then it has to be recognized that ovulation plays an insignificant part in the disappearance of ova, and a few more or a few less follicular cycles in any one year make no material difference to the duration of reproductive life. Of the 30,000 to 50,000 ova generally estimated to be present in the ovaries at puberty not more than 450 are destined to be lost by way of ovulation.

Statistical inquiries into matters raised in this question are difficult because they depend so much on the patient's memory of past events—and this tends to be unreliable. Nevertheless, they have been attempted from time to time, and the results go to show that the age of the menopause is not significantly related to either previous menstrual or previous reproductive function. Nor is it related to the age of the menarche. Of all the possible factors which have been considered, the only ones (other than disease) which most authorities would accept as likely to have any bearing on the age of the menopause are an inherited disposition manifested among races and families, and possibly social and economic status.

Male and Female Symbols

Q.—*What is the origin of the symbols ♂ and ♀?*

A.—The origin of ♂ for male and ♀ for female is from the well-known symbols of the planets, ♂ being for Mars and ♀ for Venus. Thus they come to indicate masculine and feminine qualities respectively. Very early—perhaps before the Christian era, but certainly soon after—the planetary symbols became associated also with certain metals, ♂ standing for iron and ♀ for copper. Thus they entered alchemy, where we need not follow them. How much older than the Christian era are these signs for planets it is hard to say. The association of deities with planets was borrowed from Mesopotamia by the Greeks in the 4th–5th century B.C., and later by the Romans. Thus Roman Venus corresponded to Greek Aphrodite, who corresponded to Babylonian Ishtar, the Ashtaroth of the Bible. It would therefore not be surprising if these planetary (and sexual) signs, or something like them, were ultimately traced to the second millennium B.C. In any event they are extremely ancient. One idea is that ♀ represented a hand-mirror—the "looking-glass of Venus"—and corresponded to the Egyptian *ankh*, ☥ "the handled cross," the sun's gift of life, but all such stories—and there are many—are mere fancies, unverified and perhaps unverifiable.

Borax for Cholera

Q.—*Is there any authority for the belief that borax is effective in the treatment of cholera?*

A.—There is no reliable evidence that borax is of any value in the treatment of cholera.

Testosterone into the Scrotum

Q.—*Is there any valid reason why small injections of testosterone propionate (5 mg. in 1 ml. of oil) should not be given into the scrotum? It seems to me that there might be economy by this procedure. I have a case of testicular atrophy following mumps, and the cost of normally disposed treatment is high.*

A.—There is no advantage in injecting testosterone propionate into the scrotum. The dose would not be diminished by giving it by this route, since the amount provided in a case of testicular atrophy should be roughly equivalent to the amount of testosterone produced by the normal testis. Testosterone has no effect on the atrophic testis itself.

"Any Questions?" Book.—The second book of selected "Any Questions?" is available, price 7s. 6d. (postage 6d.). Copies may be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

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